DIAGNOSIS AND TREATMENT OF ESSENTIAL HYPERTENSION

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ESSENTIAL hypertension remains a common cause of premature death. Modern treatment has improved the prognosis. But treatment is still difficult, and logically, once begun, it should be continued for life. The dilemma therefore is obvious.

The opinions expressed in this paper are based on ten years' experience of running a clinic for patients with hypertension. They have been reached after much discussion with a succession of registrars who have helped in this work—particularly Dr. C. P. Lowther and Dr. A. H. Kitchin.

Since 1948, when ganglion-blocking drugs were first received for trial, we have had no doubt that in many cases symptoms have been relieved, retinopathy cleared, left ventricular hypertrophy decreased, the recurrence of cardiac failure postponed, and life prolonged. It is also probable, though difficult to prove, that serious complications have been prevented or at least delayed. However, we also feel (1) that many patients with a raised blood-pressure are being treated unnecessarily, and (2) that the treatment of many is inadequate. Patients are often first seen at hospital because they have developed some serious complication during inadequate treatment. In our opinion it is seldom wise to begin treatment without a thorough assessment, and this means admission to hospital.

Definition of High Blood-pressure

For practical purposes, a resting blood-pressure which is consistently 160/100 mm. Hg, or higher, is abnormal at any age. This of course does not imply that it is of serious significance, or that treatment is required, or that the patient should be told of the finding. Indeed, a pressure of 160/100 is, by itself, unlikely to cause symptoms or to be associated with objective evidence of hypertensive diseases.

Whether or not hypertension is significant can often be decided only after a period of observation.

Systolic and Diastolic Hypertension

Hypertension which is principally due to a rise in the systolic pressure may occur with anxiety, aortic incompetence, thyrotoxicosis, or heart-block, but is most frequently attributable to atherosclerosis decreasing the elasticity of the aorta and its main branches. (This also tends to lower the diastolic pressure, thus increasing the pulse pressure.) As a rule, systolic hypertension does not require treatment with potent drugs, and it should be remembered that when the blood-pressure of atherosclerotic patients is lowered they are particularly liable to cerebrovascular accidents from thrombosis.

Diastolic hypertension is due to increase in the peripheral resistance, and it is with diastolic hypertension that this paper is concerned.

High Blood-pressure and Hypertensive Disease

There is as yet no actual evidence that, in patients whose only abnormality is a moderately raised blood-pressure, treatment will prevent complications in later life. Because of the long course of benign essential hypertension, such evidence cannot in any case be available for many years. It is clear, however, that if treatment is to be safe and effective close observation is necessary, and introspection is inevitable. It is also clear that no hypotensive drug is really satisfactory; indeed none is without troublesome or potentially serious side-effects.

In our view many patients with high blood-pressure do not require treatment with potent drugs. We have an increasing number of patients, mainly middle-aged women, who have been under observation for 5–20 years and have remained well without treatment, though their blood-pressure, whenever recorded, has always been of the order 230/130. It is surprising how often even such a pressure as this will fall to within the normal range with simple rest in bed. In particular we think that high blood-pressure in the elderly should not be treated unless it is definitely *causing* symptoms. We believe that most patients with only high blood-pressure should be reassured but usually kept under observation. The object of keeping in touch with them is as much to ensure that they do not receive unnecessary treatment as to ensure that they are treated appropriately and in good time if this proves necessary.

By hypertensive disease is meant objective evidence of changes, secondary to hypertension, in brain, retinæ, heart, or kidneys.

Diagnosis

The diagnosis of primary or essential hypertension can be made only after excluding conditions to which the raised blood-pressure may be secondary. In general, the younger the patient the more thorough should be the search for some underlying cause, especially if there is no family history of hypertension. Secondary hypertension is most commonly due to renal disease. Sometimes it is due to coarctation of the aorta, phæochromocytoma, or Cushing's syndrome, and occasionally to rarer conditions such as polyarteritis nodosa or aldosteronism which will not be discussed.

Renal causes of hypertension include glomerular nephritis, chronic pyelonephritis, polycystic kidneys, and various forms of unilateral renal disease associated with ischæmia—e.g., hypoplasia, pyelonephritis, tuberculosis, and obstruction of the renal artery.

Pyelonephritis is the condition most often missed and is probably the commonest cause of " malignant " hypertension. This possibility should be considered in every case, especially if there is a history of renal infection, renal pain or aching in the loin, dysuria or frequency of micturition, general malaise, or obscure febrile illnesses, and if there is any abnormality in the urine, or anæmia, or a raised erythrocyte-sedimentation rate. In such cases repeated cultures of the urine should be made, and we have found much help from renal biopsy. The detection of infection is very important because the condition is serious and often requires vigorous treatment for a long time.

Coarctation of the aorta will not be missed if one forms a habit of palpating the femoral arteries whenever high blood-pressure in the arms is recorded. If the femoral pulse is weak, or delayed after the radial, evidence of a collateral circulation should be sought by palpating around the scapulæ and in the axillæ while the patient is bending down, and by examining a radiograph of the chest for notching of the undersurfaces of the ribs.

Phæochromocytoma is suggested by paroxysmal hypertension, bouts of severe headache, palpitation, sweating, nervousness, vomiting, abdominal pain, paræsthesiæ, pallor, or fever. In the absence of such symptoms persistent hypertension is very rarely due to a phæochromocytoma, and tests for this are necessary only when specially indicated.

Cushing's syndrome is suggested by a plethoric appearance with obesity confined to the trunk and face, hirsutism of male distribution, purplish abdominal striæ, amenorrhœa, impotence, and muscular weakness.

All these possible causes for hypertension emphasise the need for initial assessment in hospital.

Ætiology of Essential Hypertension

Heredity is undoubtedly an important factor. Ayman (1934) found that where one parent has hypertension, the incidence in the children (in later life) is about 30%, and where both have hypertension it is about 45%. Thus the absence of a family history in a patient with hypertension should lead to a particularly careful search for some underlying cause—e.g., in the kidney.

Although in many people the blood-pressure rises with emotion, and emotional stimuli usually cause larger rises in blood-pressure in hypertensives than in normotensives, there is no evidence that essential hypertension is *primarily* a psychological disorder; and in general the type of psychological treatment the patient with high blood-pressure requires is no more than the general advice and sensible management from which he would benefit quite apart from hypertension.

It has been suggested that essential hypertension is no more than the upper limit of the normal distribution curve for blood-pressure in the population. However, from the clinical standpoint there are difficulties in accepting this view, and most workers think that essential hypertension is probably a disease entity, the primary cause of which is more likely to be found in the secretions of the kidney than in the nervous system. Indeed, in view of the evidence for a hormonal mechanism, it is remarkable that at present treatment is almost entirely directed to reducing nervous tone.

Classification

It is customary to divide patients with essential hypertension into benign or malignant groups. This is unsatisfactory not only because of difficulties in definition but because no indication is given of the severity of so-called benign hypertension. It seems illogical to label as "benign" the hypertension of a person whose disease is so grave that he may shortly die from cardiac failure or a cerebrovascular accident.

What has to be decided in each case is whether the patient merely has high blood-pressure or whether there is evidence of secondary hypertensive disease. If there is such evidence, one should decide whether the hypertension is mild, moderate, or severe, and:

1. As regards the *heart*, whether there is left ventricular hypertrophy, left ventricular failure, congestive cardiac failure, or associated ischæmic heart-disease (i.e., coronary disease).

2. As regards the *retina*, whether there is papillœdema, hæmorrhages, exudates, or arteriolar changes.

3. As regards the *brain*, whether there has been a major vascular accident or recurrent minor strokes or mental changes.

4. As regards the *kidneys*, whether there is evidence of renal disease, of impaired renal function, or of renal failure.

These changes are considered in detail below.

Taking the Blood-pressure

With different techniques, widely different pressures may be obtained in the same patient. Pressures vary with the degree of relaxation, posture, size and position of cuff, right or left arm, and the number of times the cuff is inflated. It is important to remember the effect of emotion in raising the blood-pressure, especially at the first visit to a new doctor. (Emotion may be responsible for a considerable rise of diastolic as well as systolic pressure.) It should also be remembered that a standard cuff (13 cm.) used on an obese arm may give a reading 15 mm. too high, and on a thin arm 15 mm. too low, and that the pressure in the two arms may differ by as much as 20 mm. in health and by more than this if hypertension is present.

The patient should be lying down, comfortable, and as far as possible relaxed. The cuff should be applied to the arm so that the bag is on the inner side—i.e., over the artery, and inflated to a pressure well above that at which the radial pulse is obliterated. The systemic pressure should be recorded as that at which the sounds first appear during deflation. It is best to record two diastolic pressures—i.e., when the sounds change and when they disappear. The arm used should be stated, and also the number of times the cuff is inflated. Thus

R4=240/130/125

signifies that at the fourth reading on the right arm the systolic pressure was 240 mm. Hg and the diastolic pressure 130 or 125 according to the point chosen. By these means greater accuracy is ensured and serial records by different observers are more comparable.

Because of these variable factors, little reliance can be placed on single, isolated, "casual" blood-pressure readings, especially when they are taken by different observers. The variation cannot be eliminated by precision in technique but it can be reduced. Blood-pressure recordings must be assessed in broad perspective.

In patients under treatment with ganglion-blocking drugs the blood-pressure *must* be recorded both in the lying and in the standing positions. Lying pressures alone are valueless, because these drugs have little if any central effect and their action mainly depends on posture.

In addition to casual blood-pressure readings, basal and sleeping pressures should be recorded.

Basal blood-pressure.—By a basal reading is meant a reading obtained in bed after a night's rest.

Sleeping blood-pressure.—If the patient is not to wake when the cuff is inflated, adequate sedation is required. This is best achieved in the evening so that natural sleep can follow. Sodium amylobarbitone or other barbiturate drug should be given in divided doses until the patient does not stir when the pressure is recorded. A mere sedation pressure—i.e., after a dose of amylobarbitone insufficient to produce sleep—is of no particular value.

The value of the test is limited because amylobarbitone lowers the cardiac output somewhat and therefore also the blood-pressure. Nevertheless it provides useful additional information and should always be carried out. A pressure which does not fall with sleep is an ominous finding.

After casual and basal pressures and a sleeping pressure have been recorded, the physician will have a fair idea of the range of blood-pressure during the 24 hours. For assessing the effect of a drug, single casual readings are useless, and a much better notion can be obtained by a "run-through" in a clinic—i.e., hourly pressures recorded by a doctor or technician. From the readings

obtained "average daily blood-pressure" can be estimated.

Multiple readings of the blood-pressure are necessary but time-consuming, and the medical staff may be inadequate for the purpose. In such cases there is no reason why a technician or nurse should not be trained to take the pressures; and, indeed, a uniform technique and comparable readings are more likely to be attained in this way than by a succession of doctors.

In some countries patients are trained to record their own blood-pressure and to modify the dose of their drug in accordance with a chart. We do not approve of this, partly because the method does not suit some temperaments and partly because such readings are not always reliable and the patients are under less close supervision than when attending a clinic. Moreover we have not found it necessary or wise to make frequent adjustments of dosage from hour to hour or day to day.

General Symptoms

Headache, giddiness, and a variety of ill-defined complaints such as nervousness, restlessness, and irritability are the symptoms mostly commonly associated with hypertension. Sometimes it is difficult to decide whether they are directly attributable to hypertension, whether hypertension has aggravated an inherent tendency to them, or whether they are due to cerebral atheroma or to psychoneurosis. They cannot be solely related to the height of the blood-pressure, because one often finds severe hypertension (as judged by the height of the blood-pressure) in someone who is apparently in robust mental and physical health, or a multitude of symptoms in someone whose pressure is not much raised.

In most cases hypertension comes to notice either because of symptoms which are definitely related to hypertensive cardiovascular disease—such as dyspnœa, angina, cardiac failure, visual disturbances, or a cerebrovascular accident—or as a result of some routine medical examination. In our experience general symptoms are infrequent and often attributable to other causes. Sometimes, however, they precede any knowledge of hypertension and cannot be attributed to any associated condition, and it is hard to believe that they are unrelated to hypertension. In such cases the response to treatment which lowers the blood-pressure is very satisfactory. In patients with "malignant" hypertension in particular, headache may be very severe and develop before the patient is aware of his high blood-pressure.

Because of the difficulties in analysis, subjective manifestations are not a satisfactory criterion on which to judge the efficacy of a drug or operation.

The Heart

Cardiac symptoms attributable to left ventricular failure from hypertension are a strong indication for treatment with hypotensive drugs. Evidence of left ventricular hypertrophy is in itself good reason for considering treatment. If the evidence for hypertrophy is slight, treatment should not be started unless there is also some other indication; but if it is clear, or the signs are progressive, treatment will certainly be necessary. Left ventricular hypertrophy is the earliest manifestation of hypertensive heart-disease. Since concentric hypertrophy occurs at the expense of chamber volume, clinical and electrocardiographic evidence of left ventricular hypertrophy often precedes radiological evidence of enlargement.

SYMPTOMS

Dyspnœa

Undue breathlessness on exertion, followed by attacks of paroxysmal nocturnal dyspnœa, is the usual sequence. There may be pain from associated coronary-artery disease.

When *dyspnœa on exertion* is due to essential hypertension there is usually evidence of pulmonary congestion or œdema, at least after exertion, and always electrocardiographic evidence of left ventricular hypertrophy. In the absence of such objective signs the diagnosis should be suspect: the symptoms may be attributable to some other cause, such as obesity, anæmia, pulmonary disease, or anxiety. Alternatively there may be associated coronary insufficiency. In cases with coronary-artery disease there may be auricular fibrillation, a history of angina or of myocardial infarction, a degree of cardiac enlargement greater than would be expected from the hypertension alone, or the electrocardiographic pattern of bundle branch block.

Before the introduction of modern treatment for essential hypertension, attacks of *nocturnal dyspnœa* usually meant that survival beyond two years or so was improbable. In such cases there is always a considerable increase in the diastolic pressure, and other signs of left ventricular failure. Sinus rhythm is usual, triple rhythm is common, and often the venous pressure is raised. There may be a trace of peripheral œdema. An injection of mersalyl, or oral chlorothiazide, will result in a good diuresis and relief for a time from further attacks. An occasional difficulty in differential diagnosis is the patient with hypertension who also has chronic bronchitis and emphysema and may get attacks of bronchial asthma.

Cardiac Pain

Though left ventricular hypertrophy may be responsible for relative coronary insufficiency, hypertrophy by itself, however great, is unlikely to cause angina pectoris. On the other hand, angina from associated coronary-artery disease is common in patients with hypertension and is a reason for considering hypotensive treatment. In some cases, perhaps, a decrease in blood-pressure, by reducing the load on the left ventricle, will relieve angina; but caution is required, and the blood-pressure should be lowered gently, because too great a fall (e.g., from postural hypotension) may result in an exacerbation of symptoms or even myocardial infarction. At present we think that, other things being equal, angina pectoris in a patient with hypertension is an indication for lowering the blood-pressure, but that the reduction of blood-pressure should be gradual and only moderate.

SIGNS

Left Ventricular Hypertrophy

Palpation.—Careful palpation of the precordium is an excellent guide to left ventricular hypertrophy, although obesity and emphysema sometimes make the assessment impossible. Since the method is subjective, opinions will sometimes differ and borderline cases must present difficulties; but the art of palpation is still worth cultivating.

Electrocardiography.—In addition to limb leads, six or preferably seven precordial leads must be recorded.

For practical purposes a tall R with S–T depression and low or negative T waves in leads recorded over the left ventricle in any patient not taking digitalis and without anginal pain are strongly suggestive of left ventricular

hypertrophy and at the least warrant the recording of serial tracings for evidence of progression. The E.C.G. may also provide useful objective evidence of improvement with treatment. As always, it should be interpreted in the light of the clinical information. Those who have the responsibility of interpreting electrocardiograms or of initiating treatment for hypertension must, of course, be familiar with the details of the various criteria used in diagnosis.

Radiological examination is of limited value in the detection of ventricular hypertrophy. When dilatation occurs there will be obvious radiological enlargement; but usually by this time there will also be symptoms relevant to the heart.

Rhythm

Patients with uncomplicated hypertensive heart-disease usually die while still in sinus rhythm. *Auricular fibrillation* or flutter probably signifies associated myocardial ischæmia from coronary atheroma, but could be due to relative ischæmia from left ventricular hypertrophy.

Pulsus alternans, which is better detected over the brachial artery while taking the blood-pressure than over the radial artery while palpating the pulse, is always a serious sign in hypertensive heart-disease.

Triple rhythm commonly accompanies, and may precede, other signs of left ventricular failure, but in our experience is not necessarily a grave prognostic sign. In the absence of other abnormalities which might confuse interpretation (e.g., bundle branch block) it may be present for many years without clinical deterioration.

Accentuation of Aortic Second Sound

Accentuation of the aortic second sound is an unreliable sign of hypertension and may be associated with atheroma of the aorta without hypertension.

Cardiac Failure

Signs of *left ventricular failure* really amount to those of pulmonary œdema.

Signs of *congestive cardiac failure*, in the form of increased venous pressure, peripheral œdema and enlargement of the liver, usually follow but occasionally precede paroxysmal dyspnœa and are evident when the patient is first seen.

Sometimes cardiac failure may be responsible for *proteinuria* or a *raised blood-urea*, which will regress when the failure responds to treatment; but often these changes signify severe secondary renal damage.

Brain

Since the effects of hypertension cannot always be distinguished from those of cerebral atheroma, and these two pathological processes are often associated, they will be considered together.

Pathological changes include hæmorrhage, thrombosis, infarction, and cerebral softening. Whether spasm of cerebral vessels occurs in essential hypertension is problematical, but it has been demonstrated that attacks of hypertensive encephalopathy are associated with a sudden rise of blood-pressure and cerebral œdema. Sometimes multiple miliary lesions are found, but in other cases the changes are localised. Frequently at postmortem examination it is evident why reduction of blood-pressure by treatment has failed to improve cerebral symptoms and why they may be made worse. Partial vascular occlusion from atheroma is common, and a reduction of blood-pressure (e.g., from temporary decrease in cardiac output secondary to left ventricular failure) or a reduction of blood-flow resulting from induced hypotension will explain transient losses of cerebral function.

Hypertensive Encephalopathy

There is no agreed definition of hypertensive encephalopathy, and often the condition is difficult to distinguish from a minor cerebrovascular accident due to hæmorrhage, thrombosis, or transient ischæmia. This term should in any case be confined to attacks of acute cerebral disorder accompanied by symptoms such as headache, vomiting, disturbance of vision, confusion, and convulsion or loss of consciousness—sometimes with transient loss of other cerebral functions, but without residual signs in the nervous system once the attack has subsided. These attacks are associated with a rapid rise in systemic pressure and also with cerebral œdema. Such attacks are of serious omen, and when it can reasonably be concluded that cerebral thrombosis has not occurred they constitute a strong indication for treatment with hypotensive drugs. Hypertensive encephalopathy is often misdiagnosed and is rare.

Cerebral Hæmorrhage and Thrombosis

The great majority of patients with cerebral hæmorrhage have high blood-pressure, and in most of them vascular disease is an associated factor. Since premonitory symptoms are common, it may well be that occlusion of a small vessel, or an area of cerebral softening, or possibly angiospasm, precedes rupture of the vessel wall. Where a cerebral vascular accident is believed to be due to hæmorrhage and a good recovery has occurred, it is reasonable to advise prophylactic treatment with hypotensive drugs; but in many cases the first cerebral hæmorrhage is fatal or crippling and often one cannot determine whether the incident is due to thrombosis or hæmorrhage. The mode of onset and the appearance of the cerebrospinal fluid are not always reliable guides. This is unfortunate because the anticoagulant drugs which would be suitable for thrombosis might well aggravate hæmorrhage, while the hypotensive drugs which might decrease the tendency to hæmorrhage might well increase the tendency to thrombosis. Hence many physicians prefer not to use either method of treatment in such cases. On the other hand there are many patients with hypertension who have a transient vascular accident attributed to cerebral thrombosis but have no other signs to suggest that cerebral atheroma is widespread. If such people show definite signs of hypertensive disease (e.g., in the retina or heart), prophylactic treatment to lower the blood-pressure is reasonable—especially if there have been other transient attacks, or premonitory symptoms, or if there is a family history of cerebral hæmorrhage.

Minor vascular accidents may be due to small areas of hæmorrhage or thrombosis or to transient reduction in cerebral blood-flow. Recognisable syndromes may result from ischæmia in the area of the internal carotid, basilar, or cerebellar arteries. In this latter group atheroma is the probable cause, and to lower the blood-pressure may be dangerous.

Major vascular accidents may result in death, hemiplegia, or monoplegia.

Mental Changes

Patients with hypertension may have diffuse cerebral atheroma which is reflected clinically as emotional lability, defective memory, changes in intellect, personality, or habits, or difficulty with speech or control of sphincters. Such symptoms are definite contraindications to treatment with hypotensive drugs. They will be made worse.

Retinæ

Disturbances of vision may be secondary to hypertensive retinopathy or may be the result of a retinal vascular accident which is primarily due to associated vascular disease. At other times, such changes are found at routine examination following the discovery of high blood-pressure. Retinopathy is often, and rightly, used as a guide to prognosis or as an indication for treatment directed to lowering the raised pressure. However, there is much confusion over terminology and considerable difference of opinion about the significance of the various ophthalmoscopic changes which may be present.

It has become customary to grade certain retinal changes according to the classification of Keith, Wagener, and Barker (1939):

Grade I.—General narrowing of the arterioles with varying calibre and increased light reflex.

Grade II.—Further reduction in calibre and constriction of the veins where crossed by the arterioles.

Grade III.—The addition of exudates and/or hæmorrhages.

Grade IV.—Papillœdema.

This classification served a useful purpose in emphasising the importance of retinal changes in diagnosis and prognosis; but in some respects it has outlived its usefulness, and paradoxically it has led to lack of precision in observation and to misinterpretation as regards significance for the individual patient. It is by no means uncommon for the physician—let alone the student—to play for safety: having detected hypertension and the absence of obvious papillœdema, hæmorrhages, or exudates, he records "fundi grade I–II", irrespective of the changes actually present, and sometimes without knowing just what these grades signify. In the face of high blood-pressure some observers lack the courage to state that the vessels are normal, although they often are.

The authors of this classification cannot be blamed for misquotation; but often hæmorrhages and exudates without diffuse arteriolar changes are recorded as grade III, though they may be the result of retinal vascular accidents from primary degenerative changes unrelated to the modest degree of hypertension which may be present. In some cases these changes are not of serious significance and do not in themselves indicate the need for hypotensive drugs.

The borderline between grade-I changes and the upper limit of normal is necessarily ill defined and they are difficult or impossible to distinguish from "senile arteriosclerosis". Grade-II changes may result from hypertension but may also be found in the elderly without hypertension, and patients showing them may live long enough to die in old age from some unrelated condition. The younger the patient the more significance must be attached to them—especially if the changes are bilateral and diffuse.

Despite these difficulties it is necessary to examine the fundi carefully and to record the various abnormalities present in each quadrant of both eyes. The pupils should be dilated and adequate time allowed. Much will be missed if the examination is confined to a hasty glance through undilated pupils.

Papillœdema may be due to the hypertension or to increased pressure from intracerebral hæmorrhage.

Hæmorrhage and exudates when accompanied by diffuse arteriolar changes are attributable to the hypertension.

Narrowing and *straightening* of arterioles is important, but unless well marked it needs considerable experience to recognise, because in the minds of many observers there is no clear range of normal. One way of assessing arteriolar calibre is by the arteriovenous ratio (usually about 4 : 6). However, branching of vessels varies from person to person, and between the eight quadrants in the same person; so, to estimate narrowing, one *must* examine vessels of comparable branching. Without a retinal camera to record objectively, it is hard to be certain of the changes which may occur from time to time. However, when definitely present, narrowing and straightening are valuable signs especially in the younger patients.

Variations in bore—i.e., changes in calibre along the course of an arteriole—are more easily recognised, not being dependent on some absolute standard. It is highly improbable that such variations are often caused by "spasm" (see below), as commonly thought. Narrow areas may be due to an organic change in the intima which decreases the lumen, while wide areas may be due to dilatation secondary to fibrosis, as emphasised by Leishman (1957). The walls of such relatively wide portions of the vessel will be thin, with a resultant reddened appearance. Such appearances, when seen in hypertensive patients, may be the result of secondary vascular changes; but in some degree they can also occur with or without hypertension, from primary degenerative changes.

Arteriovenous crossing changes in the form of constriction, concealment, or displacement of the veins have a similar significance to variations in bore; and being, like the latter, relatively free from subjectivity should be regarded as the main changes to be observed.

Tortuosity, although often mentioned, is a much misunderstood sign and varies greatly among normal people. It is of no significance whatever as regards hypertensive retinopathy.

Changes in the vessel wall may also result in broadening of the light reflex and are responsible for so-called silver and copper wiring, and also for sheathing, by which is meant a white streaking on either side of the red column of blood. These effects indicate a high degree of sclerosis but are difficult to relate to the prognosis of hypertension.

We are sceptical about the frequency of *spasm*. Hypertension of course depends on an increase in vascular tone, and this is greater in some parts of the body than in others. Spasm of the retinal vessels may occasionally occur in acute conditions such as toxæmia of pregnancy and nephritis, or in young people with transient blindness, but its occurrence in chronic hypertension is doubtful. At all events our observations indicate that narrowed regions along the course of any one vessel are usually due to organic changes in the wall which narrow the lumen or to relatively narrow areas between widening of the vessel from fibrosis. Such narrowed areas have not been seen to "dilate" in patients treated with hypotensive drugs who have been observed regularly over a considerable period. In our experience grade-I and grade-II changes rarely regress. It is therefore better to avoid the term "spasm" and refer to areas of absolute or relative narrowing.

All this is not to deny that patients who have retinopathy as well as high blood-pressure are less likely to do well than those with normal fundi, nor that when there are hæmorrhages and exudates as well as arteriolar changes the prognosis is usually relatively bad. True hypertensive retinopathy is usually a strong indication for instituting hypotensive treatment. Nevertheless in the individual patient such changes do not necessarily mean that treatment is desirable. The decision whether or not to use hypotensive drugs should be made on the sum of all the evidence.

The Kidneys

In hypertensive cardiovascular disease functional insufficiency is evident much earlier in heart, retina, or brain than in the kidneys: such symptoms as breathlessness, disorder of vision, and disturbance of higher cerebral function occur before nocturia, proteinuria, or hæmaturia, and before any change is detectable in the urea-clearance and specific-gravity concentration tests or the level of the

blood-urea. Though a change in renal hæmodynamics, with increasing impairment of renal function, is a feature of essential hypertension, most patients will die of cardiac failure or a cerebrovascular accident. In fact those who die from renal failure have usually passed into what is sometimes described as the " accelerated phase " (malignant hypertension).

The earliest change in the kidney is a reduction in renal blood-flow. Glomerular filtration, however, is maintained and hence there is an increase in the fraction of plasma filtered by the glomeruli. These changes cannot of course be detected by the ordinary tests of renal function used in the wards.

The limitations of routine laboratory tests such as the urea-clearance and the specific-gravity or dilution tests *must be appreciated.* As usually carried out, they are often inaccurate and misleading. If they are to be used for assessing the severity of hypertensive disease or as a guide to progress or to the response to treatment, precision and uniformity in technique and a recognition of their potential errors is essential. Also one must remember that proteinuria and impairment of renal function may be due to associated cardiac failure and may improve or clear up with appropriate treatment.

It is important not to subject the patient to unnecessary tests and not to overburden the laboratory with time-consuming estimations. It is better to understand and carry out a few tests thoroughly. As a reasonable guide to the degree of impairment of renal function, a *properly conducted* specific-gravity concentration test, an estimation of creatinine clearance, and (for the assessment of renal failure) the estimation of the blood-urea are all that is required. Indeed, for most practical purposes, examination of the urine and a simple estimation of the blood-urea is often sufficient, since this will show whether there is renal failure—i.e., failure of the compensatory mechanisms. If the blood-urea level is above 100 mg. per 100 ml., only symptomatic treatment should be given.

Pyelography

Before initiating medical or surgical treatment of hypertension in a patient under the age of 50, intravenous pyelography should be carried out to assist in excluding renal disease and in the hope of finding evidence of a unilateral disorder which might be cured by nephrectomy. Such opportunities are rare; but, as stated above, the younger the patient the more assiduously should some underlying cause for hypertension be sought. If some abnormality is found by intravenous pyelography, cystoscopy and the collection of a specimen from each ureter should be undertaken in order to estimate the specific gravity, chloride, and urea content as tests of relative concentrating-power. Observation of indigo-carmine excretion and retrograde pyelography can also be done. Pyelography may reveal polycystic kidneys.

Renal Biopsy

Biopsy of the kidney is likely to be used increasingly, especially in difficult cases. It is not painful and with due precautions is quite safe. We have gained valuable help in regard to the diagnosis of pyelonephritis, glomerulonephritis, collagen disorders, amyloid disease, and the severity of arteriolar changes in essential hypertension where the advisability of treatment was in doubt.

Aortography

Aortography is occasionally of crucial value in the diagnosis of unilateral renal disease which may be giving rise to hypertension. It is best carried out by a catheter passed up the femoral artery.

Associated Atherosclerosis

Though atherosclerosis and high blood-pressure are often associated there is no reason to suppose that they have a common basis. The more carefully patients with high blood-pressure are analysed, the more often will it be decided that vascular disease is the more important and high blood-pressure but an incidental accompaniment. Angina pectoris, intermittent claudication, retinal or cerebrovascular accidents, and diffuse mental changes are evidence of important vascular disease. It is true that these pathological processes may be accelerated by hypertension and that a reduction of blood-pressure might be beneficial for this reason; but it is also true that a sudden or profound lowering of blood-pressure may cause deterioration perhaps precipitating visual impairment, myocardial infarction, angina pectoris, cerebral thrombosis mental symptoms, or renal failure.

(*To be concluded*)

ISOLATION OF VIRUS FROM INCLUSION BLENNORRHŒA

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AN abacterial form of ophthalmia neonatorum has long been recognised (Kroner 1884). In 1909 both Stargardt and Schmeichler demonstrated inclusion bodies, similar to those of trachoma, in the conjunctival epithelium of some of these cases. Shortly afterwards Halberstaedter and Prowazek (1909) found similar inclusions in epithelium from the urogenital tracts of the mothers; they were also demonstrated in the urethras of several male patients with non-gonococcal urethritis (Fritsch et al. 1910, Lindner 1910). The term inclusion blennorrhœa seems to have been first used by Lindner (1909b), and we shall use this expression to designate infections of the genital tract and of the conjunctiva of the newborn. Inclusion conjunctivitis (Thygeson 1934) is the most satisfactory name for infection of the eye in later life which is acquired by contact with discharge from the infected conjunctiva or genital tract—either directly or in swimming-pools.

The infective agents of inclusion blennorrhœa and trachoma have long resisted all attempts to culture them in the laboratory. John and Hamburger (1938) claimed to have isolated the ætiological agent of inclusion blennorrhœa by inoculation of the chick-embryo chorio-allantois, and Braley (1947) described a " variant virus " that multiplied in mouse brain, but these findings have not been substantiated. Recently, however, viruses were isolated from cases of trachoma (T'ang et al. 1957, Collier and Sowa 1958) and identified as the cause of the disease (Collier and Sowa 1958, Collier, Duke-Elder, and Jones 1958). These viruses were isolated by inoculating conjunctival scrapings into the yolk sacs of embryonate eggs. In view of the close morphological resemblance between

the inclusion bodies of trachoma and those of inclusion blennorrhœa it seemed likely that a similar virus could be isolated from the latter by yolk-sac inoculation.

This paper records the isolation, in two independent laboratories, of virus from the cervix of a mother whose baby developed inclusion blennorrhœa, and from the eyes of another baby with the disease.

Family 1

THE BABY

A girl aged 13 days was admitted to Moorfields Eye Hospital on June 30, 1958, with mucopurulent conjunctivitis of the left eye of 10 days' duration. The conjunctiva was red, œdematous, and diffusely infiltrated; the cornea appeared normal on examination with the loupe. Rapid improvement took place under intensive local treatment with aureomycin, chloramphenicol, and streptomycin, and the baby was discharged on July 4, 1958.

Laboratory Investigations

Bacterial cultures from the conjunctiva made before starting treatment yielded no growth.

Conjunctival scrapings were not obtained until about 2 hours after local treatment had begun. Stained by the Giemsa-May-Grünwald method they showed epithelial cells and an inflammatory exudate of polymorphonuclear leucocytes, lymphocytes, some plasma cells and macrophages. Many of the epithelial cells were enlarged as a whole and showed vacuolation of both cytoplasm and nucleus with loss of the normal chromatin pattern. Within the cytoplasm of some of the more normal epithelial cells were typical small or large Halberstaedter-Prowazek inclusion bodies. In other cells there were inclusions containing greatly swollen elementary bodies of the type commonly seen during treatment with antibiotics.

THE MOTHER

Towards the end of pregnancy this primipara, aged 22, had a moderate vaginal discharge which persisted in spite of local treatment. Inspection 23 days after parturition (day 23) revealed a patulous fissured cervix in normal position with a moderate amount of mucopus in the vaginal vault. The cervix bled when scrapings were taken. On day 35 and day 156 discharge was still present, and mucopus was again visible on the cervix and in the vaginal vault. On both occasions scrapings from the inflamed and roughened area of the external os were examined microscopically, and were injected into eggs in attempts to isolate virus.

Laboratory Investigations

First examination (day 35).—Cervical smears stained with Giemsa-May-Grünwald showed normal epithelial cells, with fairly numerous polymorphonuclear leucocytes and erythrocytes. A smear from the posterior fornix showed masses of degenerate epithelial cells, with many red cells and bacteria. No cytoplasmic inclusions were found. Examination of iodine-stained smears for inclusions was not practicable, because the epithelial cytoplasm stained intensely by this method.

Embryo inoculation.—Cervical scrapings were collected in bottles, each containing 0·5 ml. 0·85% saline and 20,000 μg. streptomycin to inhibit bacterial contaminants, and were inoculated into 7-day chick embryos. The result was negative.

Except where otherwise stated, this method of treating epithelial scrapings for embryo inoculation was used throughout.

Second examination (day 165).—Cervical smears stained with Giemsa-May-Grünwald showed many epithelial cells, fairly numerous polymorphonuclear leucocytes, moderate numbers of lymphocytes, and occasional large mononuclear cells. Masses of bacilli were present. The epithelial cells mostly appeared normal, but occasional basophilic intracytoplasmic bodies were seen. These somewhat resembled Lindner's initial bodies (Lindner 1909a), but they were always homogeneous in structure.

Isolation of Virus at the Lister Institute

Cervical scrapings were collected in three bottles, each containing 0·5 ml. saline. 2 hours after collection the contents, which had been kept on ice throughout, were pooled and ground in a ten Broeck tissue grinder. The resulting suspension was centrifuged in the horizontal head at 1000 r.p.m. for 1 min. The supernatant was removed, and 0·4 ml. of streptomycin solution (100,000 μg. per ml.) was added. Immediately afterwards, four 7-day embryos each received 0·4 ml. of this material by the yolk-sac route. Of these two died on day 12 and two on day 13 after inoculation. No virus was present in one of the latter, but yolk-sac smears from the other three embryos contained numerous elementary bodies similar to those of trachoma virus. This agent was designated LB1.

Isolation of Virus at the Evans Biological Institute

Cervical scrapings were collected in streptomycin-saline and despatched from London packed on ice. They were kept at 0°C until, 48 hours later, they were inoculated into the yolk sacs of four 10-day and six 7-day embryos. Five eggs became contaminated by bacteria and were discarded. Two 7-day embryos examined 6 days after inoculation appeared normal. One 10-day and two 7-day embryos died on the 10th day after inoculation and showed hæmorrhagic skin lesions. The yolk sacs from these were pooled, emulsified and passed to eight 6-day embryos. Four died within 24 hours and were discarded; the remainder died between day 5 and day 11 after inoculation. All showed skin hæmorrhages, and scanty virus particles were seen in the yolk sacs of two. These sacs were pooled and inoculated into a further three 6-day embryos, two of which died 8 and 10 days later. Both were hæmorrhagic, and numerous elementary bodies were found in stained yolk-sac smears.

Family 2

The mother, a primipara, gave no history of leucorrhœa before or during pregnancy. 22 days after delivery scrapings were unsatisfactory because the cervix was still patulous, fissured, and discharging lochia.

THE BABY

A girl aged 14 days was seen at Moorfields Eye Hospital on Nov. 11, 1958, because for 3 days she had suffered from a mild recurrence of a bilateral mucopurulent conjunctivitis. It had begun 3 days after birth and had been apparently cured by 4 days' local chloramphenicol. The conjunctiva was moderately red, œdematous, and diffusely infiltrated. For diagnostic purposes the baby was treated with streptomycin drops. During the next 7 weeks the slight mucopurulent discharge steadily decreased, although during the 1st week the left eye became more inflamed. In the 8th week minute follicles could be seen with the loupe in the lower fornix, although the discharge had almost ceased. The cornea has remained clear to examination by the loupe.

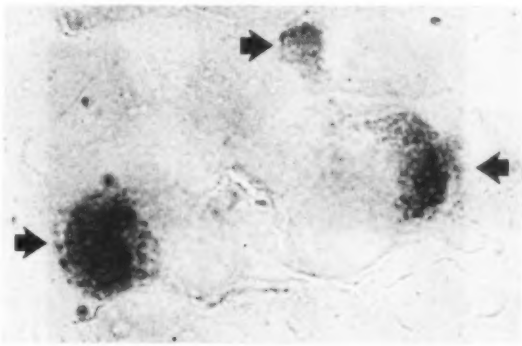

Fig. 1—Baby 2. Conjunctival scraping Lt eye (day 18) showing three Halberstaedter-Prowazek inclusion bodies stained with iodine to demonstrate carbohydrate matrix (×1200).

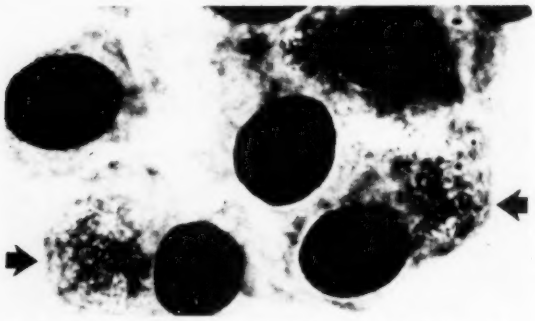

Fig. 2—Baby 2. Same field as fig. 1 after decolorisation and restaining with Giemsa-May-Grünwald to show the elementary bodies within the inclusions.

Laboratory Investigations

Bacterial cultures from the conjunctiva on day 14 yielded no growth.

Conjunctival scrapings on day 15 consisted of epithelial cells, some of which showed the changes observed in Baby 1, polymorphonuclear leucocytes, lymphocytes, some plasma cells, and macrophages. No inclusions were found. The findings were similar on day 16, but on day 18 moderate numbers of typical Halberstaedter-Prowazek inclusions were present. These were shown to have a carbohydrate matrix by the method of Gilkes, Smith, and Sowa (1958) (figs. 1 and 2).

Isolation of Virus at the Lister Institute

Conjunctival scrapings from each eye were collected separately in streptomycin-saline. These were kept at 4°C for 3 to 4 hours and then injected into the yolk sacs of three 7-day or 8-day chick embryos. By this method, virus was isolated by direct inoculation from the right eye on day 16, from both eyes on day 24, and from the left eye on day 36. An attempt made on day 29 failed because of bacterial contamination of the eggs. The virus isolated was designated LB2. At each isolation yolk-sac smears contained numerous elementary bodies morphologically similar to LB1.

Isolation of Virus at the Evans Biological Institute

On day 36 conjunctival scrapings were collected in streptomycin-saline. Since they were sent unrefrigerated from London by post, 84 μg. of polymyxin B was added to each bottle before despatch, and a further 17 μg. of polymyxin B was added just before inoculation. It was hoped thereby to minimise the risk of bacterial contamination.

The scrapings were inoculated into four 6-day embryos. Two of these were discarded because of contamination; the remaining embryos died 11 days after inoculation, and numerous elementary bodies were seen in yolk-sac smears. They were morphologically similar to those observed at the Lister Institute.

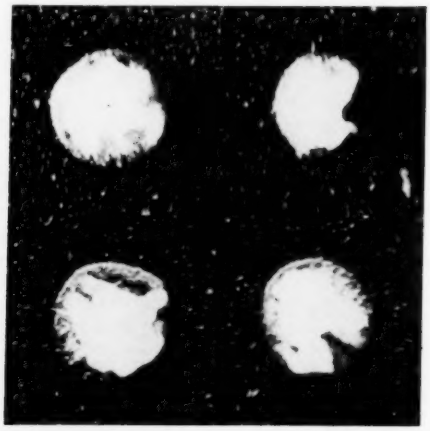

Fig. 3—Palladium-shadowed electron micrograph showing elementary bodies: (a) virus LB1; (b) virus LB2 (×55,000).

Description of the Virus

Morphology

When stained, the particles appeared to range from about 0·25 μ to 0·50 μ in diameter. With Giemsa, the larger forms stained purple and the smaller forms pink. The elementary bodies stained blue with Castañeda's stain, and red by Machiavello's method. In addition to the free virus particles, occasional closely packed aggregates of virus surrounding a central vacuole were observed with LB1 but not with LB2. These aggregates appeared identical with those produced by two strains of trachoma virus, G16 and G17, isolated in West Africa (Collier and Sowa 1958, Collier 1959). These agents have now been passaged repeatedly in the yolk sac. The embryos usually die from 7 to 9 days after inoculation. Most appear normal, but some show hæmorrhages at the insertions of the feather shafts.

Both viruses were purified by the method previously described (Collier and Sowa 1958) and fixed in 5% formalin. Electron microscopy revealed elementary bodies (fig. 3), identical in appearance with those of trachoma (Collier and Sowa 1958), and with other members of the psittacosis-lymphogranuloma group. As prepared for electron microscopy, the elementary bodies were 0·3–0·4 μ in diameter.

COMPLEMENT-FIXATION TITRATIONS OF LYMPHOGRANULOMA SERUM WITH DIFFERENT STRAINS OF VIRUS

Antigen	Titre of lymphogranuloma serum
LB1 (1/8)	1/512
LB2 (1/8)	1/512
Trachoma (Gambian strain G1) (1/8)	1/256
Trachoma (Chinese strain TE55) (1/8)	1/256
Psittacosis (1/4)	1/256
Normal yolk sac (1/8)	<1/32*

* Lowest dilution tested.

Serological Reactions

Like trachoma these viruses contain the complement-fixing antigen of the psittacosis–lymphogranuloma group (see table). Antigens were prepared and tested against serum from a case of lymphogranuloma using the methods described by Collier, Duke-Elder, and Jones (1958). A preliminary titration determined the optimum concentrations of the antigens used in the test. Doubling dilutions of serum were tested, starting at 1/32.

Serum from Mother 2 was tested against these antigens, but no complement-fixing antibody was detected even at a dilution of 1/4.

Inoculation of Baboons

A 20% suspension of yolk sac infected with strain LB1 which had undergone eight egg passages, was prepared in phosphate-buffered saline (Dulbecco and Vogt 1954) and inoculated into four young baboons (*Papio papio*) by firmly rubbing the right upper tarsal conjunctiva and fornix with a small cotton-wool swab soaked in the suspension. The left eyes were similarly treated with suspension that had been heated at 100°C for 15 min.

Before inoculation three of the animals had a few follicles in the upper fornices of the type associated with "non-specific folliculosis" commonly seen in apes. Conjunctival scrapings made just before inoculation contained epithelial cells and moderate numbers of polymorphonuclear leucocytes, lymphocytes, and plasma cells.

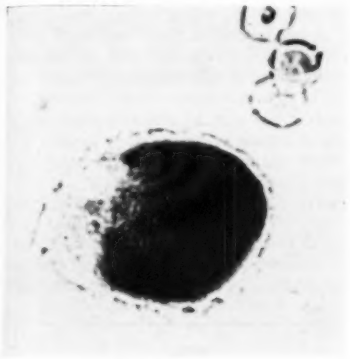

Fig. 4

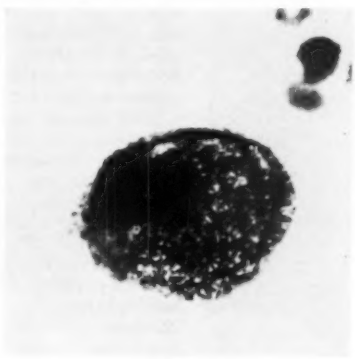

Fig. 5

Fig. 4—Conjunctival scraping from baboon inoculated with strain LB1 (day 4). Epithelial cell containing a large inclusion stained with iodine (×980).

Fig. 5—Conjunctival scraping from baboon inoculated with strain LB1 (day 4). Same field as fig. 4 after decolorisation and restaining with Giemsa-May-Grünwald. The granular inclusion almost completely replaces the cytoplasm (×980).

4 days after inoculation there was no change in the appearance of the left eyes, or in the cytology of conjunctival scrapings made from them. The conjunctivæ of the right eyes were congested, œdematous, and exuding mucopus. Conjunctival scrapings revealed degenerative changes in some of the epithelial cells and inflammatory exudate consisting of numerous polymorphs and lymphocytes, and moderate numbers of plasma cells and macrophages. Conjunctival scrapings from the right eyes of all four animals contained numerous typical Halberstaedter-Prowazek inclusions, which when stained by iodine proved to have carbohydrate matrices (figs. 4 and 5). Myriads of free elementary bodies were present, lying between the cells.

This investigation will be reported in detail elsewhere.

Discussion

The elementary bodies of the two viruses, LB1 and LB2, described in this paper are morphologically indistinguishable from those of egg-adapted trachoma virus (Collier and Sowa 1958). With LB1, the clumps of virus particles which surround vacuoles and which stain intensely with iodine cannot be distinguished from those seen in yolk sacs infected with G16 and G17 strains of Gambian trachoma virus. Furthermore, the present virus shares a complement-fixing group antigen with the viruses of trachoma and other members of the psittacosis-lymphogranuloma group.

The possibility that G16 and G17 might in fact be viruses of inclusion blennorrhœa is excluded by two facts; each was isolated from a patient with trachoma exhibiting both pannus and conjunctival cicatrisation; and G17 produced clinical trachoma, with keratitis proceeding to pannus, in a human volunteer (unpublished observation). The independent isolation of apparently identical viruses in two laboratories, one of which was not working with Gambian trachoma virus, eliminates the possibility of contamination by G16 or G17.

It is noteworthy that the virus is resistant to polymyxin B in a concentration of 167 μg. per ml. even when combined with streptomycin 40,000 μg. per ml. In subsequent isolations of virus from adults with inclusion conjunctivitis this mixture has successfully inhibited degrees of bacterial contamination that had spoilt several previous attempts with streptomycin alone. It is also of interest that LB1 survived transport on wet ice for 48 hours and LB2 survived, unrefrigerated, in the post for 24 hours, although the elementary bodies of LB1 did not appear in any numbers until the third egg passage.

Final proof that the viruses described in this paper are ætiologically related to inclusion blennorrhœa must await the results of experimental inoculations of human volunteers. However, in view of their close similarity to trachoma virus and of the successful inoculation of baboons with LB1, such a relationship may be reasonably inferred.

It is commonly held that trachoma and inclusion conjunctivitis can be clearly distinguished on clinical grounds, and by cytological examination of conjunctival scrapings (Thygeson 1955, 1958). Their ætiological agents are separated taxonomically by Bergey (1957) into *Chlamydia trachomatis* and *Chlamydia oculogenitalis* respectively. Our own observations indicate that the clinical distinction between trachoma and inclusion conjunctivitis is not always so clear as has been stated. This evidence, together with an account of viruses that we have isolated from borderline cases in adults, will be presented in a subsequent communication.

We hope that this work will serve as the basis for further study of the relationship between trachoma, inclusion blennorrhœa, and inclusion conjunctivitis of adults. Such a study may well be of great importance in elucidating the epidemiology of trachoma and allied diseases.

Summary

Viruses have been isolated from a woman with inclusion cervicitis and from a baby with inclusion blennorrhœa.

In their morphology and staining reactions these agents resemble the viruses of trachoma and other members of the psittacosis-lymphogranuloma group, with whom they share a complement-fixing group antigen.

One of these agents has been inoculated into baboons, and has induced severe inclusion conjunctivitis. This is good presumptive evidence of its ætiological relation with this disease.

We are indebted to Dr. Robin Valentine (National Institute of Medical Research) for the electron micrograph; to Dr. John Newsome (Medical Research Council Bilharzia Research Group) for providing facilities for baboon inoculation; to our colleague Mr. Peter Reeve for performing the complement-fixation titration; and to Prof. C. F. Barwell (London Hospital) for the psittacosis antigen and lymphogranuloma serum.

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ULCERATIVE COLITIS AND CARCINOMA COLI

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MUCH has been said about the psychosomatic origin of peptic ulceration and of ulcerative colitis, and about the use of psychotherapy in their treatment. But by the time these patients are admitted to a surgical department they usually have such grave organic changes that removal of one or other ætiological factor is no longer important. From this stage there are striking similarities in the course of peptic ulceration and ulcerative colitis—namely, the life-threatening bleeding, the stenosis, and the malignant degeneration.

We have treated a great number of ulcerative-colitis patients over many years, but we have found difficulty in planning systematic therapy, especially as regards the indications for surgery. Experience gained over the past five years seems to show that the risk of cancer is very high, and that when deciding whether to advise operation greater attention should be paid to this fact.

Statistically the incidence of cancer in ulcerative colitis is 3–4%; Svartz and Ernberg (1949) quote a figure of 4·3%, and Lagercrantz (1955), in children only, 4·4%. Kirsner (1957) found that the incidence of cancer in all patients with ulcerative colitis is 1·5–3·5%, in the surgical cases 4–8%, and at necropsy 15%.

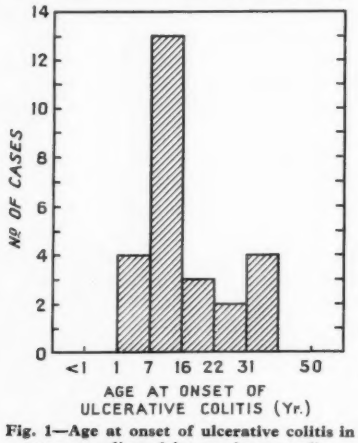

Fig. 1—Age at onset of ulcerative colitis in cases complicated by carcinoma coli.

The improved conservative treatment of ulcerative colitis with antibiotics and blood and plasma transfusions is likely to produce a state of chronicity; and this is one of the prerequisites for malignant change. The facts are that the likelihood of cancer increases with the duration of ulcerative colitis, and that cancer complicates the truly chronic cases.

Among patients who had had ulcerative colitis for ten years or more 25–50% had cancer (Cattell and Colcock 1955), 45·5% (Counsell and Dukes 1952), 36% (Lyons and Garlock 1951), and 28% (Bacon 1958). Observations on a group of 150 ulcerative-colitis patients from our pædiatric department point in the same direction (Lagercrantz 1955). In none of these had cancer developed during the first ten years of the disease, while in those followed for eleven to twenty-two years the incidence of cancer is now 33·3%:

Period of observation (yr.)	*Total no. of cases*	*No. of cancer cases*	*No. of deaths from cancer*
0–2	150	0	0
2–6	137	0	0
7–10	77	0	0
11–14	59	1	0
15–22	24	7	7

Several children with ulcerative colitis were, at the age of 15, transferred to the medical department where in the past eighteen years about 500 cases of ulcerative colitis have been treated. Some patients in whom cancer developed were also admitted direct to the surgical department from provincial hospitals. Thus, our total number of cases of verified cancer in ulcerative colitis is 26.

15 of these patients were males and 11 were females. The age at onset of symptoms is shown in fig. 1; most became ill with ulcerative colitis before the age of 15, and the mean age at onset was 16·9 years. These figures suggest that cancer developed more frequently in patients who got colitis in childhood than in those who became ill in adult life. But there may be no real difference since the cases starting in childhood were observed longer. The increase in the incidence of cancer with the duration of illness is seen in fig. 2; only 1 patient had had symptoms of ulcerative colitis for less than seven years, and most had had them for ten years or more. The average duration of symptoms was 15·4 years.

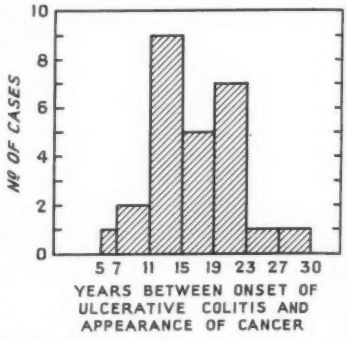

Fig. 2—Relation between ulcerative colitis and carcinoma coli.

Fig. 3 shows the age at which cancer was diagnosed. The mean was 32·3 years. Cancer as a complication of ulcerative colitis appears therefore twenty-eight years earlier on an average than any other colonic or rectal carcinoma (mean age 60 years, according to Hultborn 1952) in Sweden.

When the diagnosis of cancer was established, there were already considerable changes. In 6 patients the diagnosis was made because of intestinal obstruction. In 8 others the first evidence of cancer was severe pain, which is unusual as a symptom in ulcerative colitis. The pain may have been due to incipient obstruction.

23 patients underwent laparotomy. In 9 of these, and in 3 not operated upon, metastases were found in the liver or peritoneum. The tumour could be resected in only 11, and only 4 are still alive. The figures for mortality from cancer in our series (22 deaths within a year of the discovery of cancer among 26 patients) agree with the published reports of 77–97% (Bacon 1958).

1 of the 4 survivors in our series became ill with ulcerative colitis at the age of 10 in 1932, and she spent many years in hospital. At 26 she was diagnosed as having cancer of the transverse colon; this was resected. A year later total colectomy with ileostomy was performed, and during the next year the rectum was removed. She is still alive, ten years after the cancer was discovered, and is doing full-time work as a laboratory assistant.

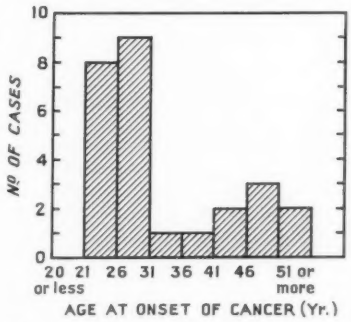

Fig. 3—Age at onset of cancer in cases of ulcerative colitis.

These observations, showing that malignant changes must often occur in young people who have had ulcerative colitis for ten years or more, and that nearly all of them die from their cancer, are bound to alter fundamentally our therapeutic

approach to ulcerative colitis. Because the cancer is so highly malignant, it would be ideal to plan a prophylactic operation, the risk of cancer being a strong addendum to the other indications for surgery. Since it would be impossible for all ulcerative-colitis patients to be operated upon, however, an analysis of cases might help in deciding which patients are especially exposed to the risk of cancer.

It has been questioned whether polyps predispose to cancer in ulcerative colitis, especially since Dukes (1954) found that the average duration of ulcerative-colitis symptoms and of familial intestinal polyposis before the development of cancer is about the same—namely, fifteen years. Dukes' observation is confirmed by our findings (fig. 2). But polyposis, pseudopolyposis, or pseudopapillomatosis were by no means demonstrated in all our cases of cancer. At colectomy performed for indications other than cancer, we found different types of polyps, which microscopically did not show any signs of malignancy. Accordingly, we do not think that cancer in ulcerative colitis is usually preceded by the formation of polyps.

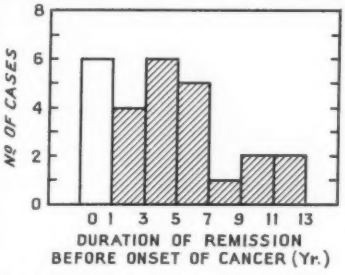

Fig. 4—Duration of remission (complete or incomplete) in cases of ulcerative colitis before onset of cancer.

The question remains whether some other characteristic in chronic ulcerative colitis could indicate the threat of malignant change.

In 1949 Svartz and Ernberg published an important observation about the malignant degeneration in ulcerative colitis. They found that most of their 9 ulcerative-colitis patients with malignant changes were young people who had been completely or almost symptom-free for a long time before the appearance of cancer. This was characteristic of practically all our 26 cases; the cancer was not the culmination of an increasingly severe progressive course, but appeared after prolonged quiescence of the diarrhœa. The data about the symptoms are largely based on the patient's own statements. As Alm and Ihre (1958) pointed out, this information should be critically assessed, since patients with ulcerative colitis frequently dissimulate. In most cases, however, there were objective signs of improvement, and in some there was radiographic evidence also.

Fig. 5—Ulcerative colitis and carcinoma.

Short colon without flexures, and with generally reduced distensibility. In the distal part of the transverse colon there is a local irregular narrowing due to malignant change.

We wish to draw particular attention to those patients who had been completely free from symptoms for several years, and had practically forgotten their existence. It will be seen (fig. 4) that 19 of the 26 cancer patients had a completely or relatively symptom-free interval of a year or more before the appearance of cancer; the longest symptom-free interval was twelve years. The explanation of this remarkable course may be that in the colon, during the perpetual inflammatory regeneration, atypical cells are produced in the mucosa. Because of this process of repair, ulceration with hæmorrhages and secretion of mucus—and therefore the typical symptoms—cannot be as severe as before.

Fibrous hardening of the colonic wall must cause shrinkage of the entire colon, which should be seen in the radiograph not only as a reduction of the lumen but as a shortening of the whole organ.

The X-ray findings could be accurately assessed in 24 of our cases. In 17 the colon was found to be oval in shape and shortened without flexures. In 4 the loops were preserved. In these and in the 3 other cases there was, at the time of diagnosis of cancer, a decrease of the radiographic appear-

(a)

(b)

(c)

Fig. 6—(a) Ulcerative colitis in a 9-year-old boy.

Short colon without flexures, and with reduced distensibility. There are no sacculations; the outlines are irregular.

(b) 10 years later.

The colon is longer and there is greater distensibility; there are no sacculations and the outlines are more even.

(c) After a further 6 years.

The colon is still longer; in the distal part of the transverse colon there is narrowing of the lumen, nearly 10 cm. in length and with irregular outlines, of malignant origin.

ances of ulcerative colitis as compared with earlier X-ray examinations.

Thus, it is clear that cancer can appear in cases of ulcerative colitis in which there is radiological as well as clinical improvement. Permanent shortening of the colon might possibly be interpreted as a precancerous state, but at present we cannot be certain. On the other hand, it may be that such shortening of the colon is usual and can be seen for a long time in patients with ulcerative colitis even when cancer does not follow. The X-ray findings in our series will have to be compared with those in the ulcerative-colitis patients without cancer from the rest of the hospital.

Fig. 7—The localisation of cancer in 26 cases of ulcerative colitis.

To summarise our experience, we may say that the radiological diagnosis of fully developed cancer is seldom difficult. Some typical films from 2 of our cases are shown in figs. 5 and 6. We would stress the importance of including X-ray examination in the regular check-up of patients who have or have had ulcerative colitis. Continued investigation and analysis of chronic cases will in time settle the question of the extent to which permanent shortening of the colon or other radiographic appearances should be considered in deciding whether a " cancer-preventing " colectomy is indicated.

We shall not discuss here the principles of surgical treatment of ulcerative colitis. Most surgeons are now convinced that total colectomy with ileostomy generally gives a good therapeutic result. An ileostomy, however, is by no means ideal for young patients. Ileostomies involve considerable risk of severe disturbances of fluid balance, and of the development of fistula and prolapse, although these risks have been much reduced by modern techniques (Brooke 1954, Crile and Turnbull 1954). Further, in many patients, removal of the whole rectum will interfere with normal sexual functions. Many surgeons are now trying to use more moderate procedures, with preservation of the rectum for later operations to restore continence. In assessing a technical procedure of this kind the risk of the development of cancer must, of course, also be taken into consideration. Since ulcerative colitis nearly always starts in the recto-sigmoid, the severe organic complications arise mainly in this area. Accordingly, many authors think that total proctocolectomy should be performed (see Bacon 1958).

In 24 of our 26 cases the cancer was in the upper part of the colon, and in only 2 was it at the rectosigmoid junction (fig. 7). In performing colectomies for cancer we have therefore felt justified in preserving the rectum so as to be able later to undertake ileorectal anastomosis. In 2 cases of ulcerative colitis with cancer and several cases without cancer we have in recent years performed colectomy and ileoproctostomy in one stage with good results.

If the rectum is preserved, however, it must be borne in mind that cancer may be expected to develop later, and these patients should be carefully followed up for the rest of their lives. Boddington and Truelove (1956) have shown also that in relatively early cases of ulcerative colitis the rectal mucosa contains atypical cells which have certain features in common with malignant cells.

Summary

Among patients who have had ulcerative colitis for ten to twenty years, 1 in 3 develops carcinoma coli. An account is given of 26 patients with this complication, of whom only 4 survived.

Since the cancer is highly malignant and difficult to diagnose, colectomy is indicated as a prophylactic measure.

Relative freedom from the symptoms of ulcerative colitis does not imply that cancer will not develop. On the contrary, most of our patients were completely or almost symptom-free for several years before the appearance of cancer.

The possibility of assessing radiologically the indications for a " cancer-preventing " colectomy is discussed.

Because the cancer in most cases involves the upper part of the colon, colectomy and ileorectal anastomosis should be considered.

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THE EFFECT OF NEOMYCIN ON PHAGE-TYPING OF STAPHYLOCOCCI

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Loss of phage sensitivity on contact with antibiotics, followed by reversion to the original pattern, does not seem to have been reported in a clinical investigation. In a series of in-vitro experiments, however, Barber (1957) found that after long-continued subculture penicillin-resistant mutant strains of staphylococci lost their sensitivity to bacteriophage which lysed the parent strain; and that on reversion to penicillin sensitivity the organisms also regained their sensitivity to phage (Barber 1959).

We began our investigation when a member of the laboratory staff suffering from a tracheitis was found to have coagulase-positive phage-type-80 staphylococci in her nose and throat. A nasal spray consisting of neomycin sulphate 0·25% (w/v) and ' Tyrothricin ' * 0·02% (w/v) (hereinafter called N-T solution) was used in conjunction with ' Graneodin ' † ointment several times daily; and a

* A mixture of gramicidin and tyrocidin which is obtained from a crude culture extract of *Bacillus brevis*.

† 'Graneodin' (Squibb) contains neomycin and gramicidin.

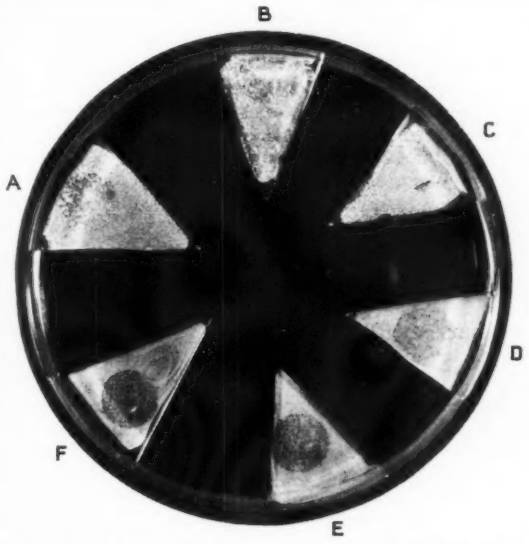

Plate showing growth of a strain of staphylococcus, type 80, previously cultured in increasing dilutions of graneodin. A: control. B-F: cultures grown in graneodin 1/800–1/2500. Lysis increases with dilution.

nasal swab four days later showed coagulase-positive staphylococci which did not type with 80 phage. After a fortnight's holiday without treatment, she again had phage-type-80 staphylococci in her nose. Since reinfection was unlikely, it was probable that the local application of antibiotics had in some way interfered with phage typing.

The Investigation

Method of Phage-typing

We use a modification of the method of Williams and Ripon (1952): our phage is supplied by the Colindale Staphylococcal Reference Laboratory.

Staphylococci from nutrient-agar plates containing 0·1 unit of penicillin per ml. are seeded into 2 ml. of digest broth and incubated at 37°C for four to five hours. A loopful of the broth culture is spread on a segment of tryptone agar enriched with 0·2 ml. of a solution containing aneurine 10 mg. and nicotinamide 100 mg. per 100 ml. of agar base. One drop of phage is allowed to fall on the dried inoculum and the plate is incubated overnight at 25°C. Plates are examined against background illumination from a microscope lamp and the presence of plaques of lysis recorded.

Investigation of Carriers

We decided to investigate changes in the nasal flora of 11 carriers of phage-type-80 staphylococcus, discovered on routine nasal swabbing of the staff. After repeated spraying with N-T solution and the application of graneodin ointment, the nasal swabs of 2 remained free from staphylococci for an indefinite period, 1 relapsed after three weeks, and the remaining 8 showed coagulase-positive penicillin-resistant staphylococci which could not be typed by the routine screening method using phages 80 and 52.

The eight strains which did not type were subcultured on three successive days into fresh serum broth. Of these five were now found to be lysed by phage 80; one gave an entirely different phage pattern and was regarded as a reinfection by a different strain, and the remaining two were not investigated further at that time. This suggested that the treatment had induced a temporary phage resistance, a phenomenon which had not been encountered during the systemic use of other drugs.

Laboratory Studies

Since it appeared likely that the topical application of N-T solution could bring about a temporary resistance to phage, we sought to find out, in vitro, whether one or both components were responsible.

Tubes of digest broth containing dilutions from 1/10 to 1/100,000 of the N-T solution were inoculated with the same amount of a freshly grown broth culture of a type-80 staphylococcus. After twenty-four hours' incubation no growth was seen at dilutions below 1/1000, moderate growth at dilutions of 1/1000 and 1/1250, and heavy growth at and above 1/1500. Organisms from all tubes in which they had grown were phage-typed. The phage failed to lyse the organisms from the tubes containing dilutions of 1/1000 and 1/1250 in which growth had been very slight. Organisms from tubes containing dilutions of 1/1500 to 1/4000 were only partially lysed. At greater dilutions lysis was complete (table I).

Next, the cultures from dilutions 1/1000 and 1/1250 were subcultured daily without N-T for three successive days in serum broth. At the end of this time the organisms had regained their previous phage sensitivity and were completely lysed by 80 phage.

TABLE II—ORIGIN OF STRAINS, PHAGE-TYPE, AND HIGHEST CONCENTRATION OF NEOMYCIN-TYROTHRICIN PERMITTING GROWTH

No.	Age	Sex	Source of staphylococcus	Phage-type	Highest concentration of solution in which organisms grew
1	37	M	Nasal swab	80/52	1/1000
2	25	M	Pus from boil	80	1/400
3	41	M	Pus from abscess	80	1/200
4	63	M	Urine	80	1/800
5	38	M	Pus from boil	80	1/1331
6	16	M	Pus from abscess	80/52	1/1331
7	56	M	Pus from boil	80	1/3200
8	32	F	Nasal swab	80	1/6400
9	29	F	Eye swab	80	1/1600
10	18	F	Pus from boil	80	1/3200
11	—	M	Pus from boil	80	1/3200
12	—	F	Tracheostomy swab	80	1/200
13	—	F	Nasal swab	80	1/800
14	27	M	Nasal swab	80/52	1/2000
15	27	M	Nasal swab	80/52	1/1000
16	8	F	Swab of septic spot	80	1/1000
17	22	F	Nasal swab	80/52	1/800
18	12	M	Nasal swab	80/52	1/1500
19	—	F	Breast milk	80/52	1/1000
20	—	M	Eye swab	80/52	1/1400

In all cases phage sensitivity was first lost but regained after three daily subcultures in serum broth.

Similar experiments were carried out on a total of nineteen other strains of type-80 and type-52 staphylococcus obtained from various sources during routine hospital investigations. These strains varied considerably in their sensitivity to N-T (table II). In all cases phage sensitivity was lost when grown at the highest concentration permitting growth but was regained after three passages in broth. A further dilution experiment was carried out using neomycin and tyrothricin separately. Table III shows that tyrothricin had no effect on phage-typing but that neomycin had precisely the same depressant effect on typing as N-T solution. Chloramphenicol did not interfere with the susceptibility to phage.

Since it was possible that loss of sensitivity to phage was accompanied by other changes in the staphylococcus, the organisms which had grown in N-T solution were tested for their

TABLE I—EFFECT OF INCREASING DILUTIONS OF NEOMYCIN-TYROTHRICIN SOLUTION OF PHAGE-TYPING OF ONE OF THE STRAINS OF STAPHYLOCOCCI TESTED

Dilution of N-T solution	1/1000	1/1250	1/1500	1/2000	1/4000	1/5000	1/10,000	1/25,000	1/50,000	1/100,000
Number of plaques on phage-typing plate..	No lysis		6	14	30	+	+	Complete lysis		

+ = plaques too numerous to count.

TABLE II!—THE EFFECT OF INCREASING DILUTIONS OF NEOMYCIN, TYROTHRICIN, AND CHLORAMPHENICOL ON THE PHAGE-TYPING OF A STRAIN OF *Staph. aureus*

NEOMYCIN (0·25% w/v)

Dilution ..	1/100	1/200	1/400	1/800	1/1600	1/3200	Control
Growth ..	−	−	−	±	±	±	+
Phage-typing	A	A	A	A	P	P	P

TYROTHRICIN (2·5% w/v)

Dilution	1/100	1/200	1/400	1/800	1/1600	1/3200	Control
Growth ..	±	±	±	+	+	+	+
Phage-typing	P	P	P	P	P	P	P

CHLORAMPHENICOL

Dilution (μg. per ml.)	20	10	5	2·5	1·25	0·625	0·3125	0·1562	0·078	0·039	Control
Growth ..	±	±	±	±	+	+	+	+	+	+	+
Phage-typing	P	P	P	P	P	P	P	P	P	P	P

A: phage-typing absent. P: phage-typing present.

ability to form free and bound coagulase (Duthie 1954) and alpha-lysin. In no instance was the capacity to produce free and bound coagulase impaired, but organisms which had become resistant to phage did not form alpha-lysin in the presence of oxygen and carbon dioxide. Alpha-lysin production together with sensitivity to phage returned after three serial subcultures in serum broth.

Discussion

Outbreaks of infection in hospitals caused by the staphylococcus, phage-type 80, are distressingly common and widespread. As the staphylococcus gradually becomes resistant to a wide range of antibiotics, the prevention and control of such outbreaks becomes more and more difficult. The role of the nasal carrier in the spread of infection has been well established. Gillespie and Alder (1957) found that barrier nursing of patients with open sepsis and the treatment of nasal carriers are of the utmost importance. Hare and Thomas (1956) have shown that nasal carriers can heavily contaminate their environment with staphylococci. Rountree and Freeman (1955) showed how the incidence of neonatal staphylococcal infections was greatly reduced by treating nasal carriers among nurses with 'Neotracin' (bacitracin and neomycin).

The routine nasal swab is widely used in hospitals to detect carriers. They are then treated with graneodin ointment or N-T solution and are allowed to resume normal duties if the swabs grow staphylococci other than the epidemic strain or one which fails to type. If the organisms become resistant to phage-typing while retaining their pathogenic properties those dealing with an outbreak and the carriers themselves may develop a false sense of security.

Our experience is that, in vivo, staphylococci may become resistant to antibiotics such as streptomycin, chloramphenicol, or erythromycin, given systematically without losing their phage susceptibility. This may not be so when N-T or graneodin is applied topically in the nose or when the organisms grow in vitro in minimal inhibitory doses of the drug. In both cases phage sensitivity is lost, but it is regained on subculture and (we believe) on cessation of treatment. Gillespie and Alder (1957) state that "relapse after graneodin, with the reappearance of the same strain, does not often happen provided treatment is continued for at least a week after the swab becomes negative". Our finding, on the contrary, was that coagulase-positive staphylococci which did not type appeared even after several weeks of negative plates; and they proved to be type 80 after three daily broth subcultures.

We therefore suggest that nasal carriers from whom type-80 staphylococci have been isolated should not be regarded as clear merely because, after treatment, their organisms fail to type. Such staphylococci should be subcultured three times in broth and the phage-typing should then be repeated.

Summary

Following 'Graneodin' and neomycin-tyrothricin treatment of the anterior nares, swabs taken from 8 of 11 nasal carriers of type-80 staphylococcus grew coagulase-positive staphylococci which could not be phage-typed. 5 of these 8 regained their sensitivity to phage after three daily subcultures in broth.

When type-80 staphylococci from various sources were grown in increasing concentrations of neomycin-tyrothricin solution and neomycin alone, the bacteria which grew in the highest concentrations lost their phage sensitivity. As with organisms from treated nasal carriers, sensitivity was regained after three daily subcultures in nutrient broth.

Similar experiments with chloramphenicol and tyrothricin did not affect phage-typing.

Since ointments and solutions containing neomycin are now widely used in the treatment of nasal carriers, there is a danger that the true nature of a strain may be overlooked when it fails to type. We therefore suggest that if, after neomycin treatment, a previously virulent strain of coagulase-positive staphylococcus cannot be typed, the organism should be subcultured in broth or established as having another phage pattern.

We wish to thank Dr. E. S. Duthie for his very helpful criticism and advice, and Mr. J. Wilcox, A.I.M.L.T., for the photograph.

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MARKING-INK POISONING
AN OUTBREAK OF METHÆMOGLOBIN CYANOSIS IN NEWBORN BABIES

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UNCOMMON hazards are apt to escape recognition when they occur, so that diagnosis and life-saving treatment may be delayed. In retrospect it is seen that, however well the senior staff may have been aware of the possibility years ago, information has not reached all the present members of a team. They may be totally unaware of any risk, or of the reasons for administrative safeguards which have long been in force. Such a hazard is aniline-dye poisoning of babies by unfixed marking-ink, which can convert the hæmoglobin of the red corpuscles into methæmoglobin to an extent which endangers life.

The Outbreak

In a maternity home of twenty-two beds six neonates were affected simultaneously with cyanosis. In five cases this was mild and symptomless, and disappeared within 24 hours. One baby, however, who was the first to show cyanosis, and who was placed in an oxygen-dome for this reason, was severely affected and displayed cerebral irritation and prolonged twitching while being treated. In this case intravenous methylene-blue was given with dramatic and complete recovery of normal colour.

The First Case

The severely affected baby came of a twin first pregnancy and was the second twin, born by the breech without difficulty, weighing 5 lb. 14 oz. (2670 g.). Vitamin K, 1 mg., was injected at birth, as is our routine in complicated deliveries. Initially, he showed blue asphyxia which disappeared promptly on clearing the air-passages.

His twin, who was born by the vertex, died aged 2 days after a cyanotic attack; the cause of death was certified as atelectasis, but no necropsy was held. There was no marking-ink hazard up to the time of this baby's death.

The baby made normal progress until 8 days old, when he weighed 5 lb. $9^1/_2$ oz. (2540 g.) on Dec. 22, 1957. On this evening at 8.50 he became cyanosed and passed a fluid green stool which shot out explosively. Cyanosis deepened and he was placed in an oxygen dome at 11 P.M. Shortly after midnight his colour was grey, and he became more cyanosed during feeding; some twitching was noticed and chloral hydrate, gr. 1, was given. He passed another loose stool and 'Kaomycin', drachm 1 (4 ml.), was given at 2 A.M. on Dec. 23. A third loose green stool was passed at 3.30 A.M. He was tube-fed at 3.30 A.M. and at 10 A.M., as he appeared to be listless, and intramuscular penicillin (100,000 units) was given.

At 11 A.M. on Dec. 23 he was transferred to the children's ward of Moorgate Hospital, Rotherham. By this time his colour was a most peculiar greyish-black and his lips, ears, feet, and hands looked as if they had been dipped in blue-black ink. There was no dark smudge on his skin of staining by marking-ink. He showed no distress or breathlessness. His cry was normal and strong. The ribs were not drawn in and there were no abnormal heart signs. He was alert and moved actively. His fontanelle was slightly depressed. His temperature was 103·4° and no focus of infection was found in his mouth or throat, ear drums, chest or abdomen, except that the umbilicus was moist with some purulent discharge. A swab from this yielded a heavy mixed growth of *Staphylococcus pyogenes*, *Escherichia coli*, and *Streptococcus fæcalis*, all of which were sensitive to all the broad-spectrum antibiotics. The baby was unnaturally jumpy and started at sudden noises, but there were no grossly abnormal signs in the central nervous system. Blood examination showed hæmoglobin 16·0 g. per 100 ml., red blood corpuscles 4,800,000 per c.mm., white blood-cells 17,700 per c.mm. (neutrophils 36%, lympohcytes 54%, monocytes 10%). The reticulocyte-count was 4%. The blood sample taken for grouping was very dark in the syringe, darker than pure venous blood. Spectroscopic examination showed intense absorption bands of methæmoglobin.

Ascorbic acid 200 mg. was given by mouth, and methylene-blue 5 mg. was injected intravenously. The baby's colour began to improve almost immediately after the methylene-blue injection, and within a quarter of an hour his skin had an entirely normal pink colour. The suddenness of colour change inclined us to credit the response to the intravenous methylene-blue, and not to the ascorbic acid by mouth. Sedation with phenobarbitone gr. $^1/_8$ (8 mg.) was given 8-hourly.

On the next day, Dec. 24, the baby's colour remained normal, but he would not suck. There was twitching of his face and eyes and a whining cry. The bowels moved very freely five times during the day, and the temperature came down to normal. Twitching and refusal to suck continued throughout Dec. 25, and then ceased. Thereafter recovery was uneventful, and phenobarbitone sedation was stopped on Dec. 30. His hæmoglobin was 12·4 g. per 100 ml. on Jan. 10, 1958. His development was subsequently normal, and on July 29, 1958, when $7^1/_2$ months old, he weighed $19^1/_2$ lb. and was taking a mixed diet.

The Other Cases

Five other babies in the same maternity home were also found to be mildly cyanosed when examined on the morning of Dec. 23. None of them required any specific treatment, apart from removal of the source of intoxication when this was discovered. Their colour returned to normal within 24 hours.

Source of Poisoning

At this maternity home all napkins have for some years been marked by a sewing-machine, and the use of marking-ink had long been discontinued. However, owing to a breakdown in the return of laundry, it was necessary to issue from stock 72 new napkins at 6 P.M. on Dec. 20. As the sewing-machine happened to be out of order, all these napkins were immediately marked with the maternity-home name stamp, using a bottle of old marking-ink which had been on the shelves more than 8 years. On Dec. 22, at 6 P.M. these napkins were made available for use, without being laundered first. The first baby became cyanosed by 8.50 P.M., as described above. Other newly marked napkins were used for each of the other babies who became cyanosed. Only in the first case was an oxygen dome thought to be necessary. In the dome he was subjected to the added hazard of intense rebreathing of aniline vapour, whereas the other five babies were exposed only to the chance of skin absorption and inhaling vapour as they lay in their cots.

Discussion

For 70 years this danger of marking-ink has been known, since Rayner (1886) in London reported seventeen babies with "whimberry" cyanosis due to aniline-stamped napkins in a nursery. This type of marking-ink has been reported as containing aniline dyes dissolved in aniline and nitrobenzene mixtures (Kagan et al. 1949, Howarth 1951). Direct skin absorption and inhalation of vapour have both been held responsible for intoxication.

Attention has been drawn to local staining of the buttock by contact with large black areas of unwashed napkin (Pickup and Eeles 1953, MacMath and Apley 1954). An Australian schoolboy aged 14 (Stening 1951) sat on a chemistry laboratory stool after wiping off some colourless liquid. His seat became warm and sticky, and 95 minutes later he became ill and cyanosed, and later collapsed. He was restored, after critical delay, with intravenous methylene-blue.

Inhalation is incriminated by reports of the smell of aniline, especially in the case of babies in incubators and oxygen tents (Etteldorf 1951). In our own outbreak the difference in severity between the five mild cases and the one serious case can be explained by the high concentration of volatile poison to which this baby was exposed in the oxygen dome. This route of absorption is supported by the frequency of respiratory complications in the literature (Kagan et al. 1949, Graubarth et al. 1945). Thus, five out of nine affected premature infants in one nursery developed bronchopneumonia in the 2nd to 4th weeks after exposure (Kagan et al. 1949). Kagan counted five deaths among sixty-three babies in 7 published reports.

Similar poisoning in older children has been reported as due to aniline derivatives in wax crayons, shoe dye, furniture polish, or by drinking marking-ink (Macdonald 1951).

Several reports confirm our own experience of the rapid effect of intravenous methylene-blue, which acts

by virtue of its reversible catalysis of tissue reduction and oxidation—the change from methæmoglobin to hæmoglobin being one of reduction (Wendel 1939, Scott et al. 1946, Etteldorf 1951, Macdonald 1951, Stening 1951). Ampoules of this dye should be in any hospital emergency-treatment outfit.

Administrative Comment

After this outbreak a cautionary note about aniline-dye poisoning was sent for interest to the matrons of maternity hospitals and children's departments where we work. The reply of one matron throws light on the way in which this hazard might arise. Her reaction was in effect: "Interesting—but it could never happen to us because our linen is marked by a stitching machine." This actually was also the normal arrangement at the maternity home where the poisoning took place, but the stitching machine was out of action and there had been a delay in the return of laundry—hence the hazard. It seems, therefore, that this sort of accident could happen in any hospital where there remains an old bottle of marking-ink which has not been emptied down the drain. Renewed publicity needs to be given every year to the importance of fixing marking-ink before garments are used, and this subject might be given prominence in all refresher courses for midwives.

Summary

A small outbreak of marking-ink poisoning with methæmoglobinæmia in six neonates in a maternity nursery is reported.

The one severe case responded dramatically to intravenous methylene-blue, which should be available in hospital emergency-treatment cupboards.

The hazard arose through domestic circumstances, as new members of the staff were unaware of the reason for long-standing safeguards.

We have pleasure in thanking the matron of the maternity home, Miss M. E. Johnstone; Dr. Alan Taylor and Dr. K. I. Peckitt, the practitioners in charge of the babies; Dr. H. R. Colquitt, consultant pathologist; Mr. Edwin French, biochemist; and Prof. D. V. Hubble for his advice upon this paper.

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"... In my opinion there is no basic difference between the psychopath who enriches society and the one who robs it: they are cut of the same cloth, and any apparent difference is in their goals rather than their substance.... Society has been generous in rewarding those who have made contributions to it, and has often overlooked or forgiven very serious deviations from conventional norms of behavior in the same persons. Society has been equally diligent, and with good reason, in attempting to protect itself from its asocial psychopaths. It certainly cannot afford to be complacent about them.... One need only reflect on international tensions to appreciate the menace of the predatory psychopath. Can anyone question how close psychopaths have come to the conquest and destruction of the present social order? The psychopath of tomorrow will be no different from the psychopath of yesterday: he will either enrich and create civilizations, or he will impoverish and destroy them. What he may do to society depends on what society does about him."—HARRY L. KOZOL, *New Engl. J. Med.*, March 26, 1959, p. 638.

THE ACTION SPECTRUM FOR SKIN LESIONS IN PORPHYRIA CUTANEA TARDA

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THE nature and importance of the part played by light in the production of cutaneous lesions in porphyria have long been both confused and controversial. The large literature on this subject has been critically reviewed by Blum (1941) and by Goldsmith and Hellier (1954). Clinical evidence suggests that light *is* a factor in the production of lesions, but photosensitivity has seldom been demonstrated satisfactorily. Wells and Rimington (1953), however, described convincing experimental lesions in a man with porphyria cutanea tarda. By exposing him to direct sunlight, to sunlight through window glass, or to a carbon arc, they produced œdema and ecchymoses in the skin: the mercury arc did not elicit this reaction. Rimington (1952) has suggested that photosensitivity, when present, is almost certainly due to the actual presence of porphyrins in the skin. If this is so, the wavelengths of light that will produce lesions, the action spectrum, should correspond to the absorption spectrum of the porphyrin. The most effective wavelength would be expected to lie in the region of the Soret band, 390–410 mμ, where light absorption is maximal.

Experiments designed to test this relationship have usually employed combinations of filters which would select the required region of the spectrum. Thus Riemerschmid and Quin (1941) demonstrated in the skin of sheep a correspondence between the visible absorption spectra both of eosin and of the chlorophyll porphyrin, phylloerythrin, and the regions of the spectrum most effective in producing lesions of photosensitisation. Filter combinations have many disadvantages, however, especially the difficulty of isolating a sufficiently narrow band of the spectrum.

Using a monochromator for skin tests on a patient with porphyria cutanea, we have obtained evidence strongly supporting the hypothesis that photosensitisation is due to the presence of porphyrin. The patient was the sister of the man reported in detail by Wells and Rimington (1953).

Case-report

An unmarried female of 29 had suffered from intermittent swelling of the exposed parts of the skin for the past 9 years. The swelling was principally on the back of the hands and on the face 1 to 2 hours after sufficient exposure to sunlight, and lasted about 24 hours. Sometimes the swelling was followed by ecchymoses. Blisters had occurred, though rarely, on the back of the hands, but it was not clear that sunlight was the cause. She had also suffered for about 5 years from vague abdominal colic. All these symptoms varied in severity. Her past history was not relevant and her brother was the only other member of the family with porphyria.

Biochemical progress has been followed by one of us (C. R.) by porphyrin analyses over the past 7 years. The results of these analyses are summarised in table I.

TABLE I—ANALYSES OF PORPHYRIN EXCRETION

Urinary porphyrin excretion
(Normal: up to 110–120 μg. per litre)

Date	μg. per litre	Remarks
June, 1951	47	
October, 1951	37	
January, 1953	344	
October, 1953	376	
November, 1953	614	
November, 1953	696	
Dec. 1, 1953	139	1st day of menstrual period
Dec. 2, 1953	333	2nd day of period
Dec. 3, 1953	1325	3rd day of period; indican also present in urine
September, 1958*	321	24-hour total 515 μg.

Fæcal porphyrin excretion

Date	Protoporphyrin μg. per g. dry wt. (Normal range: 0–30 μg. per g. dry wt.)	Coproporphyrin μg. per g. dry wt. (Normal range: 0–20 μg. per g. dry wt.)
June, 1951	1270	45
September, 1958*	1477	127

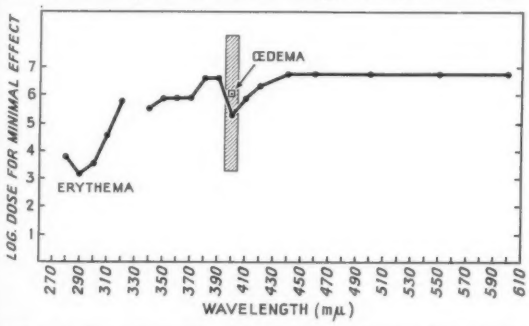
* Tests during photosensitivity investigations.

Physical examination showed no abnormalities. The skin was moderately but not abnormally pigmented. There were no cutaneous lesions suggesting porphyria. The typical fluorescence of porphyrins was obtained when the serum was viewed in Wood's light, however, but the skin and teeth did not show this. Porphyrin analyses of urine and fæces during the time of photosensitivity tests are included in table I. Both urinary and fæcal excretion of porphyrins were abnormal, the fæcal concentration of porphyrins being especially high.

Photosensitivity Tests

Tests were carried out with a large quartz monochromator using a high-pressure xenon arc as the light source.

The arc emits a continuous spectrum from the ultraviolet zone to the infra-red region, and the instrument enables light of narrow wavebands to be isolated from the ultraviolet spectrum—for instance, at 300 mμ the waveband is 3 mμ wide. In the visible spectrum the wavebands are somewhat broader, being 10 mμ at 400 mμ and wider at longer wavelengths. The test procedure was to find the minimal erythemal dose for a waveband by giving a series of exposures of graded duration. This was repeated at 10 mμ intervals in the ultraviolet spectrum from 280 mμ to 420 mμ. Tests were also made in the visible and infra-red regions at wider intervals in the spectrum. The relative intensity of the radiant energy with each waveband was measured with a Schwarz linear thermopile placed at the exit slit of the monochromator. Dosage was expressed as the product of time (seconds) and relative intensity (arbitrary units). In the action spectrum (see figure) the minimal dose is expressed in common logarithms.



Action spectrum in female aged 29 with porphyria cutanea tarda. Dose is product of time (seconds) and relative intensity (arbitrary units).

The shaded column with its centre at 400 mμ indicates the approximate range of the Soret band, the region of maximal absorption by most porphyrins. The point enclosed by a small square within the Soret band indicates the dose at 400 mμ required to produce œdema in the patient. This dose is nearly ten times higher than the minimal erythemal dose, the ordinate scale being logarithmic. The minimal erythemal dose at 400 mμ should be noted also to be over ten times smaller than the minimal dose for erythema at 390 mμ.

All the monochromator tests were made on the skin of the back. Tests were also made with light of wide waveband to which the skin of the back and of the dorsal surface of the hand was exposed, and the results in the two areas were compared.

Table II records the values of the molecular extinction coefficients at the wavelengths of the principal absorption bands of coproporphyrin dissolved in dioxan (these values have been taken from the available literature). In dioxan the absorption spectrum is of the neutral type, similar to that expected from a porphyrin in solution in body fluids. The greatest absorption is at 397·5 mμ. The molecular extinction coefficient at 297 mμ, in the normal sunburn spectrum, is also given for comparison.

Results

The results shown in the figure may be discussed conveniently by considering the action spectrum in four different regions.

At 280–330 mμ, within the normal sunburn spectrum, the patient gave results essentially the same as those found in thirty control subjects. The patient's response was a normal delayed sunburn erythema with the onset 6–12 hours after exposure. No response was obtained with exposures of up to 15 minutes at 330 mμ, as is often the case in normal subjects. Longer exposures are often necessary, but were not tried with this patient.

TABLE II—ABSORPTION MAXIMA AND MOLECULAR EXTINCTION COEFFICIENTS OF COPROPORPHYRIN TETRAMETHYL ESTER I DISSOLVED IN DIOXAN

Absorption maximum (mμ)	$E_{mol} \times 10^{-4}$	
	A	B
622·5	0·518	
621		0·515
567·5	0·678	
567		0·672
530	0·989	
529		0·997
497		1·470
496	1·492	
397·5	17·92	
297	0·872	

Column A: data calculated from figures of Brugsch and Kubowitz (1953).
Column B: data of Stern and Wenderlein (1934).

At 340–390 mμ the patient showed an early erythema—i.e., a response which appeared immediately after exposure, or within 5 minutes, and which persisted for up to 36 hours. We have often seen this type of response in normal subjects exposed to light between 340–370 mμ from doses very similar to those effective in our patient. Only two instances of erythema have, however, been seen in control subjects tested at 380 mμ, and only one at 390 mμ; slightly larger doses were necessary than those required for the patient.

At 400 mμ the patient showed an early erythema after an exposure of $^1/_2$ minute, whereas such response has not been seen in normal subjects after prolonged exposure, even up to 1 hour. The minimal dose for erythema at this point is ten times less than that required at 390 mμ. With longer exposure at 400 mμ, our patient noticed a burning or itching sensation during the test. This was followed about 2 hours later by the appearance of an œdematous swelling lasting about 24 hours. This experimental lesion seemed closely to resemble the natural one and was reproduced on six different occasions over 4 consecutive days, the dose of light required varying only slightly. On two occasions ecchymoses were seen to appear at the site of the test after some 18 hours, and on another occasion a *hæmorrhagic blister* developed 5 days after the exposure. 2 or 3 weeks later the skin at several of the test sites was pigmented, telangiectatic, and slightly atrophic, the appearance recalling the natural skin lesion.

At 410, 420, 440, 460, 500, 550, and 600 mμ the patient developed early erythema reactions. Single exposures of 15 to 20 minutes were given with each of these wavelengths. No visible cutaneous responses have been observed in normal subjects when our instrument was used in these wavelengths. *At 650, 700, 800, and 1000 mμ*, however, no response was obtained in our patient or in the controls.

Further Tests

To compare the reactivity of the skin in certain regions, light of wide waveband (from 320 mμ to about 1000 mμ) was obtained by deflecting a beam of light directly from the light source so that it did not go through the monochromator. The beam was focused on to the skin, first passing through 3 cm. of distilled water in a glass cuvette (walls 2 × 2 mm. thick) to cut out the rays producing sunburn and most of the infra-red rays. The intensity of the light was too powerful to be measured accurately with the apparatus available, but the conditions of the test were standardised as far as possible and checked each time on control subjects. In normal subjects, exposure of 10 to 20 minutes to the skin of the dorsum of the hand or of the back usually produced slight immediate erythema and occasionally direct pigmentation (" pigment darkening "), but nothing else. In the patient with porphyria, exposures lasting 5 minutes were sufficient to cause intense erythema, irritation, and later swelling and sometimes even ecchymoses. Again the experimentally produced lesions seemed to be essentially the same as those produced by natural sunlight. In some instances, as with the monochromator tests, the late effect on the skin, 2 or 3 weeks afterwards, was telangiectasia, pigmentation, and atrophy. There seemed to be no difference in the reactivity of the skin of the dorsum of the hand and that of the back.

We have recently been able to do limited tests for photosensitivity on the patient's brother (Wells and Rimington 1953). This man showed a strong immediate erythema when tested with the monochromator at 400 mμ and 2 hours later a striking œdematous lesion developed. This response was the same as that produced in his sister, but it was more marked.

Summary and Conclusions

This patient with porphyria cutanea tarda showed abnormal reactions in the skin to light of wavebands which corresponded well to the absorption spectrum of porphyrins. Abnormal cutaneous reactions—e.g., swelling, ecchymoses, and even blistering, sometimes leading later to pigmentation, telangiectasia, and atrophy—were produced at 400 mμ with a monochromator. This point is at the region of maximal absorption, the Soret band, of most porphyrins. Erythema was observed also as a result of exposures to wavebands in the visible spectrum from 410 to 600 mμ; these responses may correspond to the lesser peaks of absorption shown by porphyrins when viewed in the visible spectrum. On the other hand. the skin reactions of the patient to ultraviolet light in the normal sunburn region (around 300 mμ) were normal. Abnormal responses to light occurred as readily in skin normally clothed as in that habitually exposed.

The evidence strongly suggests that in this patient photosensitivity is initiated by porphyrins in the skin.

Thanks are due to Dr. W. N. Goldsmith, who first saw the patient and made a clinical diagnosis, for his interest and for allowing us to study his patient, and to Prof. W. D. Wright for designing and making the monochromator. We are grateful also to Dr. G. C. Wells for his help and to Mr. R. J. Lunnon for the diagrams. St. John's Hospital for Diseases of the Skin and the Medical Research Council generously made grants towards the cost of apparatus.

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HAEMOLYTIC DISEASE OF THE NEWBORN CAUSED BY ANTI-DUFFY (Fy^a)

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THE blood-group system called Duffy was reported by Cutbush, Mollison, and Parkin in 1950. In their case isoimmunisation to the antigen had resulted from numerous previous blood-transfusions. Many examples of anti-Duffy (Fy^a) have since been described, but apparently the only report of anti-Fy^a causing hæmolytic disease of the newborn is that of Baker et al. (1956). The present report describes a further instance of hæmolytic disease of the newborn apparently due to anti-Fy^a.

Case-report

The mother, Mrs. E., was known to be O, rhesus-negative, and rhesus-immunised. As far as is known she has never been transfused.

Previous Pregnancies

1938.—Premature infant. This died in a few hours.

1939.—Macerated premature infant.

1942.—Normal full-term infant. This infant's blood-group was O, rhesus-negative.

1945.—Premature jaundiced infant. A blood-film showed erythroblastosis and the infant was transfused with O, rhesus-negative, packed cells on the 1st day, but he died on the following day. His blood-group was O, rhesus-positive, (D+). After delivery the mother's serum was shown to contain rhesus antibodies.

1946.—Stillborn hydropic infant. Before delivery rhesus antibodies had been found in the serum of the mother. A direct Coombs test on the cord blood was positive. The infant's blood-group was O, cDE/cde.

Present Pregnancy

Mrs. E. became pregnant again in 1958 and in the 3rd month her serum was shown to contain rhesus antibodies active in physiological saline solution, albumin and by the anti-human-globulin technique against all rhesus-positive cells. In addition, there was an antibody which could be demonstrated only by the anti-human-globulin technique against some rhesus-negative cells. The latter reaction was weak and appeared to be due to anti-Fy^a. This was confirmed by Dr. Dorothy Parkin, of the Blood Group Reference Laboratory, where the mother was shown to be Fy (a—). At the 8th month the mother's serum gave a much more powerful reaction by the anti-globulin technique against rhesus-negative, Fy (a+) cells, and we predicted a combined incompatibility to Rh and Fy^a in the fœtus.

The infant was delivered at term by cæsarean section. Tests on the cord blood showed the blood-group to be O, rhesus-negative; the direct Coombs test was positive, the hæmoglobin 102%, and serum-bilirubin was 3·6 mg. per 100 ml. The infant became visibly jaundiced soon after birth. A replacement transfusion was given of O, rhesus-negative, Fy (a—) packed cells and the baby did well. Fy^a-typing of the infant was not done at birth as the anti-Fy^a serum available acted only by the anti-human-globulin technique. On the 64th day after delivery Fy^a-typing of the infant was attempted, but the cells reacted only weakly with a powerful anti-Fy^a serum. It was assumed that most of the cells present were still donor cells. On the 100th day the cells of the infant were shown to be Fy (a+) and confirmed to be O, rhesus-negative.

The mother's serum was tested by the anti-human-globulin technique against fourteen specimens of rhesus-negative blood and reacted only with the ten which were Fy (a+) and not at all with the four which were Fy (a—). Samples of blood from the mother and her husband were sent to Dr. R. R. Race who showed their groups to be:

Mrs. E.: O, MM.S, P_2, cde/cde, Lu (a—), K—, Le (a+b—), Fy (a—).

Mr. E.: O, Ms Ns, P_1, cDE/cde, Lu (a−), K−, Le (a+b−), Fy (a+).

Dr. Race also confirmed that the antibody acting against rhesus-negative cells was anti-Fy^a.

Conclusions and Summary

A case of hæmolytic disease of the newborn due to anti-Fy^a is described. Both the mother and infant were O, rhesus-negative, thus precluding ABO incompatibility or rhesus incompatibility from being the cause of this condition. The antibody in this instance was apparently anti-Fy^a, stimulated by pregnancy, the infant being Fy (a+) and the mother Fy (a−). The antibody could be detected only by the anti-human-globulin technique and gave relatively weak reactions against homologous cells early in pregnancy although these reactions became stronger as pregnancy advanced.

In about 22% of all matings there is a possibility of isoimmunisation by the Fy^a antigen. It should not be assumed that the only antibody present in the serum of a rhesus-negative person is anti-Rh. This case illustrates the value of testing the sera of all mothers—irrespective of their previous histories—in every pregnancy for antibodies against the commonly occurring antigens. Also, wherever possible, blood for transfusion of infants suffering from hæmolytic disease should be tested for compatibility with the mother's serum.

I am indebted to Dr. R. R. Race for blood-grouping the mother and her husband, and for confirming the presence of anti-Fy^a; to Dr. D. M. Parkin for performing the original confirmatory tests; and to Dr. R. J. Drummond, director, Welsh Regional Blood Transfusion Centre, Cardiff, for his helpful criticism and permission to record.

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HYPERNEPHROMA PRESENTING WITH INTRACTABLE HICCUP

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As is well known, hypernephroma may present in a number of ways, and the diagnosis is sometimes difficult and long delayed. Hiccup as the first symptom does not seem to have been previously recorded.

Case-report

A Service engineer, then aged 50, was first seen at the Bristol Royal Infirmary on Nov. 13, 1951. Diabetes mellitus was diagnosed and he was treated by diet. Thereafter he attended the diabetic clinic until August, 1956, when he left the district. He was well until October, 1957, when, after an attack of "influenza", he began to lose weight and feel unwell. In December, 1957, he developed a right-sided Bell's palsy, for which no cause was found; but this improved rapidly and a month later he returned to work.

On April 11, 1958, he was admitted to another hospital complaining of loss of weight and tiredness for seven months, polyuria but no polydipsia, and hiccup for three months. No mass was palpable in the abdomen; the chest X-ray revealed nothing significant; and there was no pyrexia. His blood-sugar was 265 mg. per 100 ml. and he was treated with insulin and discharged on tolbutamide on April 30. His hiccup had subsided and he had put on a little weight.

He was seen again as an outpatient at the same hospital on June 9. Although his urine was sugar-free there had been an alarming loss of weight and hiccup was very troublesome, attacks lasting for seven days and nights with only two to three days' interval. After readmission next day, investigations showed: hæmoglobin 94% and 100%; white blood-cells 6000 and 10,000 per c.mm. (normal differentials); erythrocyte-sedimentation rate (E.S.R.) 6 mm. in the first hour; blood-urea 25 mg. and 30 mg. per 100 ml.; blood-sugar 187 mg. and 237 mg. per 100 ml.; serum-amylase 10 and 8 Wohlgemuth units. Chest radiography and barium meal showed nothing abnormal. He was discharged on July 2; the weight loss had been checked and the hiccup had subsided. During his stay there had been an occasional rise of temperature.

The improvement was shortlived; hiccup returned and he could not resume work. He was therefore referred to the Bristol Royal Infirmary, where he was seen on July 29. He was thought to have an abdominal neoplasm, and a lesion of the transverse colon involving the diaphragm seemed the most likely explanation of the hiccup. When admitted on August 20, he had lost 3 st. in three months, and he was much distressed by hiccup about twice in a minute. Apart from the loss of weight, there were no abnormal physical findings. His hæmoglobin was 83%, with white blood-cells 9400 per c.mm. (normal differential), and E.S.R. 10 mm. in the first hour. No occult blood was found in three stools, and there were no significant findings with a barium enema or chest radiography. At gastroscopy on Sept. 1 nothing abnormal was seen. The total fat in the fæces was 26% of which 20% was split. The direct van den Bergh was 0·05 mg. of bilirubin per 100 ml. and the indirect 0·25. From the appearance of the pyloric antrum on barium-meal examination it was felt that there might be disease in this area—intrinsic or extrinsic.

On Sept. 12 laparotomy was performed. The pancreas was fibrotic and the left kidney enlarged, containing a tumour in its upper pole. Some infiltration of the surrounding tissue was noted and there was adhesion of the diaphragm which could have been neoplastic or inflammatory. This kidney was removed and a tumour 7 cm. in diameter was demonstrated. Sections showed cells typical of the Grawitz tumour. After operation, hiccup was continuous for a week but then became intermittent with attacks lasting about thirty minutes once or twice a day. The patient was discharged on Sept. 30.

When seen on Oct. 29 he had been free of hiccup for 5 days, and he had gained almost 1 st. in a month. The urine was normal on microscopy. On April 23 there had been no further hiccup, and his chest X-ray film was unchanged. He had returned to his original weight, and had been back at work for six weeks.

Discussion

This case illustrates the value of laparotomy where an abdominal lesion is suspected but laboratory and X-ray investigations provide little support for the suspicion. It also illustrates the difficulties, which are common, in the diagnosis of hypernephroma. Of the 40 proven cases of hypernephroma seen at the Bristol Royal Infirmary in the past eight years, 3 were diagnosed post mortem and 3 at laparotomy: in none of these 6 had the diagnosis been raised previously. Of the remainder, 6 had shown one of the classical triad—pain, hæmaturia, or a palpable mass—a year or more before the diagnosis was established. Braasch (1913) laid stress on the need to make the diagnosis before all three members of the triad were present, and this he was able to do in 51 of his 83 proven cases. He also pointed out that a proportion of cases must be missed until after metastases have appeared, and Creevy (1935) reported 37 of his 92 proven cases presenting with symptoms due to secondary deposits.

Systemic manifestations (debility, pyrexia, amyloidosis, polycythæmia) in the absence of the classical triad or evidence of secondary deposits are now recognised, and gastrointestinal symptoms are not uncommon (Berger and Sinkoff 1957). Abeshouse and Weinberg (1945) noted gastrointestinal symptoms—including nausea, vomiting, distension, eructation, vague pain, and constipation—in 11 of their 45 cases. Creevy (1935) found post-prandial epigastric distress, nausea, and vomiting to be not

unusual in his cases, and he attributed them to progressive invasion by the tumour.

The fact that our patient's hiccup subsided after nephrectomy suggests that involvement of the diaphragm was inflammatory rather than neoplastic. Surveys of 1231 reported cases of malignant renal neoplasm (Squier 1909, Judd and Hand 1929, Soloway 1938, Melicow 1944) revealed no previous case presenting with hiccup. This is surprising because perinephric invasion is common.

My thanks are due to Dr. J. E. Cates and Mr. W. M. Capper for their permission to publish details of this case.

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PALLIATION IN VAGINAL URINARY FISTULÆ

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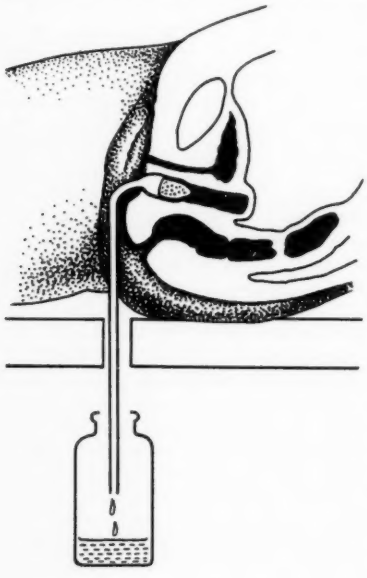
SURGICAL repair of ureterovaginal and vesicovaginal fistulæ—obstetric or postoperative—is generally postponed until local and general conditions are at their optimum, and until spontaneous healing has become unlikely. The period of postponement is usually at least one month and may be considerably longer.

If urinary incontinence is more than slight, it may require much nursing care, including frequent changes of bed linen. In spite of meticulous care, moreover, vulval and sacral skin soreness may develop.

The following simple method of collecting and draining the extravasated urine has been found efficacious.

The apparatus consists of a piece of natural marine sponge inserted into $1^1/_4$ in. Paul's rubber tubing so that approximately two-thirds of the sponge is left protruding. The sponge is thoroughly moistened and inserted with the attached end of tubing into the vagina. Usually no retaining bandage or strapping is necessary. The other end of the Paul's tubing is led into a drainage bottle (see figure). The urine is absorbed by the sponge, which is being desaturated continuously by drainage down the tubing.



In bed patients the mattress should preferably be split, so that the tubing can pass directly downwards to the drainage bottle. The method works very well when the patient sits in a chair, and, with the Paul's tubing leading into a light plastic portable urinal, it may even be satisfactory when she is walking.

The sponge is removed daily, sterilised by boiling, and reinserted.

The method has not been tried in "hopeless" cases of vesicovaginal fistulæ due to carcinoma of the cervix, with or without radiation necrosis, but it may have a place in their management when further surgical procedures are contraindicated.

Other continuous urinary fistulæ can be managed by the application of a sponge, but suction apparatus and firm tubing are usually needed to keep the sponge desaturated.

Preliminary Communications

AN AGAR-GEL PRECIPITATION TEST FOR THE LABORATORY DIAGNOSIS OF SMALLPOX

THE flocculation reaction between variola-vaccinia antigen and hyperimmune antivaccinial rabbit serum was described by Gordon [1] in 1925 and intensively investigated by Craigie and Tulloch.[2] Although the flocculation could be obtained constantly with extracts of scabs from cases of smallpox and alastrim, this tube test never came into general favour for diagnosis. Downie [3] mentions it only briefly in his review of the laboratory diagnosis of smallpox, and Kempe [4] omits it altogether.

As a diagnostic test, precipitation in agar gel by the Ouchterlony technique has two advantages over precipitation in tubes. Firstly, no clarification of the antigen is necessary. Secondly, a more immediate comparison may be made between the material under test and a positive control. A specific "line" of precipitate, formed by a test material, will bend and fuse with the corresponding line of precipitate, formed by a positive control antigen, when the precipitating antigens are identical. For this reason it is more suitable for diagnosis than the test using double diffusion in one dimension described for pox viruses by Gispen.[5] We describe the results of an agar gel precipitation test applied to samples of crusts from human cases of smallpox and alastrim. It has also been applied successfully to vesicle fluid and crusts from a recent case of smallpox in Liverpool.

MATERIAL AND METHODS

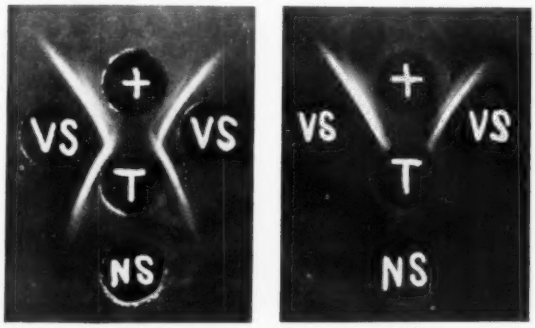
The materials we used were made available through the kindness of Prof. A. W. Downie, Dr. F. O. MacCallum, and Prof. A. Herrlich. Positive controls were provided by extracts of crusts from proved cases of smallpox. Extracts of chick chorioallantois, heavily infected 3 days previously with variola virus or vaccinia lymph, have also been used for this purpose. Negative controls will be discussed later. The precipitating serum was taken from rabbits hyperimmunised with rabbit-passed vaccinia virus. Negative control serum was taken from normal rabbits.

The technique we used followed that described by Mansi [6] with some modifications. Reservoirs 4 mm. in diameter with centres 5 mm. apart were made in an agar layer 1 mm. deep

1. Gordon, M. H. *Spec. Rep. Ser. med. Res. Coun., Lond.* 1925, no. 98.
2. Craigie, J., Tulloch, W. J. *ibid.* 1931, no. 156.
3. Downie, A. W. *Mon. Bull. Minist. Hlth Lab. Serv.* 1946, **5,** 114.
4. Kempe, C. H. Diagnostic Procedures for Virus and Rickettsial Diseases; p. 341. New York, 1956.
5. Gispen, R. *J. Immunol.* 1955, **74,** 134.
6. Mansi, W. *Nature, Lond.* 1958, **181,** 1289.

on a microscope slide. The agar was at a 1% concentration in isotonic phosphate-saline buffer of pH 7·3 containing 0·01% merthiolate.[7] Antigen extracts were made from selected scabs by extraction with phosphate-buffered saline of the same pH and molarity as that of the agar gel. Crusts were first crushed with a glass rod and then allowed to stand for an hour at 37°C with enough of the buffer to make a 5–10% suspension (w/v). The reservoirs were filled with the appropriate reagents, and the slide was kept in a humid atmosphere at room temperature.

The lines of precipitate appear in 2 hours and those from adjacent reservoirs link up 4–5 hours after the test is set up.



(a) (b)

Precipitation tests for variola-vaccinia antigen: (a) positive, and (b) negative.

T = test extract.
+ = positive control extract of variola crusts.
VS = antivaccinal rabbit serum (undiluted and 1/2).
NS = normal rabbit serum.

No anomalous reactions were found with this technique. None of a variety of negative controls, including varicella and zoster fluids, herpex-simplex scabs, and exudate from a burn, has given a line of precipitate against antivaccinial rabbit serum.

Both positive control extracts and test extracts may be treated with 0·2% formalin without diminishing their ability to diffuse and form clear lines of precipitation. This stability to formalin had been described by Craigie and Tulloch.[2] Infectivity is removed in a few hours by this treatment, and if this extra time is taken the test may be made with non-infective materials. A positive control treated with 0·2% formalin remains usable for several weeks at least. Heating crust extracts at 60°C for 15 minutes greatly weakened the strength of the reactions. Good clear positive reactions can be obtained from extracts of single crusts in 0·1 ml. of buffered saline, but these extracts cannot be diluted very far without loss of the specific reaction. As stressed by Craigie and Tulloch,[2] it is important to select compact "seed-like" crusts.

Nine samples of crusts which were available in reasonable quantity were tested in dilutions up to 1/60 (w/v). In all these tests there was a clear reaction up to 1/30, and a faint reaction was obtained at 1/60. The faint reactions from these very dilute samples were easier to see when the precipitating serum was used in a dilution of 1/2 instead of undiluted, and we recommended that two concentrations of the positive serum should be used. The samples of serum which were used gave clear precipitation up to a dilution of 1/10.

A suitable design for use as a diagnostic test is shown in the figure. In this pattern one reservoir of test antigen (T) is tested in parallel with a positive control (+) against two concentrations of antivaccinial serum (VS), and it is also checked against normal rabbit serum (NS). In the figure (*a*) shows a typical positive reaction, and (*b*) shows a negative reaction in which the lines of precipitate from the positive control disappear into the test-antigen reservoir.

7. Crumpton, M. J., Davies, D. A. L. *Proc. roy. Soc.* B, 1956, **145**, 109.

RESULTS

Stored crusts from sixteen cases of smallpox and fourteen cases of alastrim were examined by this technique. All gave positive results except those from three cases of alastrim. Each of these three specimens consisted of two very small crusts (total weight of each specimen was less than 5 mg.), and the dilution tested was 1/80 or higher. No material was left to test at a stronger concentration. All thirty specimens had been stored at 4°C for periods varying from a few weeks to 13 years.

A single sample of vesicle fluid (diluted to about 1/30) from the recent case of smallpox in Liverpool gave the positive result which is shown in the figure. Crusts from the same patient also gave a strongly positive precipitation test. The negative test shown was from the crusts of a boy with a generalised herpes-simplex infection, from whose scabs the herpes-simplex virus was recovered. Three samples of vesicle fluid from primary vaccinations, and a single stored sample of dried vesicle fluid from a case of alastrim were tested, and all four gave positive results.

A number of samples of human post-vaccination and smallpox-convalescent serum were tested against a smallpox-crust extract. Only a proportion of these gave precipitation, but all had been stored for some years at 4°C. The main use of the precipitation test, however, is for detecting antigen. For estimating antibody rise the more sensitive complement-fixation test is more satisfactory.

SUMMARY

A simple and rapid laboratory test for the diagnosis of smallpox is described.

The test depends on the demonstration of specific antigen in crusts or vesicle fluid by precipitation with antivaccinial rabbit serum, using the Ouchterlony precipitation technique.

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STERILISATION BY ETHYLENE OXIDE

FOR the many materials which cannot be sterilised by heat, sterilisation by gas is a possible alternative. Various mixtures of ethylene oxide (C_2H_4O) with different gases and vapours have been found effective under different conditions of time, temperature, pressure and humidity.[1] But, though many observations on this technique have now been published, particularly in the United States, its assessment is complicated by the wide range of variable factors, as well as by the different bacteria and methods used for testing its efficacy.

We investigated the possibility of sterilising the 'Aga' heart-lung apparatus with ethylene oxide. This machine has a cover of acrylic material (and some of the surfaces in contact with the extracorporeal circulation are also made of this), while polyvinyl chloride (P.V.C.) tubing and rubber also form parts of the apparatus.

Although a suitable large container in which the Aga apparatus could be treated was not at first available, we made preliminary tests of the efficacy of ethylene oxide

1. Sykes, G. Disinfection and Sterilization. London, 1958.

under conditions which would have practical application on a large scale.

THE INVESTIGATIONS

Ethylene-oxide/Arcton Mixture

It was decided to use a mixture of the gas with fluorocarbons as the vehicle since, unlike mixtures with air, these are not inflammable or explosive and since, unlike mixtures with carbon dioxide, they are released in constant proportions. Furthermore these mixtures are said to be effective at pressures of about 5 lb. per sq. in., whereas with gases such as carbon dioxide or nitrogen, pressures around 15 lb. per sq. in. may be required.

Two fluorocarbon compounds were used: these are manufactured and supplied by Imperial Chemical Industries Ltd. under the names 'Arcton 6' and 'Arcton 9'. The mixtures were provided in pressurised cylinders by British Oxygen Research and Development Ltd. The first batch was found to contain less than the intended strength of ethylene oxide—4% instead of 11% by weight. Tests using this weaker mixture were largely successful, however, and some of these earlier results are given. In recent experiments the mixture has been of the following composition:

Arcton 6	11 % by weight
Arcton 9	80 % „ „
Ethylene oxide	9 % „ „

Since it was found convenient to prepare the mixtures by weighing, the percentage figures are given on this basis. With the components used, a concentration of ethylene oxide of 9% by weight is approximately equivalent to 20% by volume.

Test Preparations

In the earlier experiments 5 mm. discs of cotton cloth impregnated with sporing *Bacillus subtilis* (supplied by the Southern Group Laboratory in their "Standard Sterilisation Test Envelopes") were employed. These were first used as provided but in later tests where effective penetration of the P.V.C. tubing (2·25 mm. thickness) was in question the discs were transferred to sterile glass tubes with cotton-wool plugs. In later experiments similar discs which had been freeze-dried were used for these tests. Two of these tubes with the cotton-wool plugs were then wired tightly into the open ends of a short length of P.V.C. tubing.

Since no definite correlation between resistance to heat and resistance to ethylene oxide was known, and since some workers have found *Staphylococcus pyogenes* and *Bacillus anthracis* more insensitive to the gas than several other organisms, these two species were also used in the test. Cultures of each were grown for 18 to 24 hours in 5% horse blood in broth. Using sterile forceps we moistened swabs (on shortened wood applicators) in one or other culture and transferred them to glass tubes with cotton-wool plugs. The plugs were then pushed well within the mouth of the tube and the tubes were used in this form, or inserted in pairs in the P.V.C. tubing, as described above.

Application of Ethylene-oxide/Arcton Mixture

Various patterns of McIntosh and Fildes' jar, from which the catalyst had been removed, were used in these tests. Conditions of humidity and temperature were not deliberately controlled. Ambient temperatures measured during the experiments were found to vary between 100°F and 110°F.

The ethylene-oxide/arcton mixture was introduced into the jars by first producing a vacuum of 28–29 in. (70–73 cm.) Hg and then filling from the cylinder through a valve. Initially the pressure inside the container was brought to 25 cm. Hg above atmospheric (5 lb. per sq. in.) and was measured at intervals during the test period. There was always some fall in pressure, although this varied considerably, and it was not possible to determine to what extent the fall was due to leakage from the jar and/or uptake of ethylene oxide by the P.V.C. Where necessary the pressure was restored by one or two further additions from the cylinder.

Test Cultures

Where possible, cultures were set up without delay, to avoid any continued activity of ethylene oxide after the trial period; but intervals of up to 3 hours were sometimes unavoidable.

The impregnated discs were transferred with a mounted sterile needle to tubes containing 10 ml. of nutrient broth. Infected swabs were cultured by adding 4 ml. of broth to the tubes containing them and incubated at 37°C. Visible growth from unsterilised material usually appeared after incubation for 1 day, but occasionally was not observed for 2 or 3 days. Sterility was recorded if there was no growth after 7 days and these preparations were then tested for their ability to support growth of the same organism.

RESULTS AND CONCLUSIONS

The results of this preliminary investigation are summarised in the table. Apart from the sterilisation by 9% ethylene oxide of all but one of the preparations exposed overnight (13 hours), the effective penetration of P.V.C. tubing is of special interest.

EFFECT ON DIFFERENT ORGANISMS OF EXPOSURE TO ETHYLENE OXIDE VAPOUR FOR 13 HOURS

Percentage by weight of ethylene oxide	Test preparation	Tubes with cotton-wool plugs	
		Unattached	Ends wired into P.V.C. tubing
4	*Bacillus subtilis* (dried discs impregnated with spores)	5/8*	2/6
	Staphylococcus pyogenes (swab moistened with young culture)	7/7	7/7
	Bacillus anthracis (swab moistened with young culture)	7/7	7/7
9	*Bacillus subtilis* (dried discs impregnated with spores)	9/9	9/10
	Staphylococcus pyogenes (swab moistened with young culture)	10/10	10/10
	Bacillus anthracis (swab moistened with young culture)	10/10	9/9

* Number showing no growth/number tested.

There are two possible disadvantages of sterilisation by ethylene oxide which will need further investigation. First, solution of 15 mg. of ethylene oxide from vapour can occur in 1 g. of rubber,[2] and slow release of the gas into the circulation could possibly produce an undesirable concentration of ethylene glycol in the blood—even though the Aga machine is flushed with warm glucose saline before use. Secondly, the possibility of a deleterious effect of ethylene oxide on different materials is also important and has not yet been studied fully. No visible alteration was observed, however, in samples of various substances which were tested in the jars as follows:

Polyvinyl (P.V.C.) tubing.
Acrylic sheet ('Perspex').
Plastic dental prostheses.

We are very grateful to Mr. M. K. Aspinall, instrument room supervisor at The London Hospital; to Dr. A. Bracken and Mr. C. C. Wilton-Davies of British Oxygen Research and Development Ltd. for much help and advice; and to Mr. J. G. Chapman for the laboratory preparations and tests.

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2. Royce, A., Moore, W. K. S. *Brit. J. industr. Med.* 1955, **12**, 169.

Medical Societies

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

THE 79th annual congress was held in London, at the Royal Society of Medicine, on April 9–11. Over 300 members and their guests attended, including several distinguished foreign visitors. Mr. R. C. DAVENPORT, president of the society, was in the chair. In his presidential address on glaucoma he considered the relationship between myopia and glaucoma, recalling that association of the two conditions was not as rare as was often supposed, and he discussed the connection between glaucoma and obliterative arterial disease and its possible ætiological significance.

Swollen Optic Disc

Mr. DESMOND GREAVES emphasised the need to recognise the wide limits of normal and congenital anomalies of the optic disc and to distinguish them from early pathological changes. He discussed the vascular arrangement at the nerve-head, and the absence of any considerable connection between the central artery of the optic nerve and the circle of Zinn on the one hand and the central retinal artery on the other. The relationship between the degree of swelling of the optic disc and the loss of function gave much help in diagnosis. In the discussion all agreed that papillœdema was an unsatisfactory term, especially for universal application to the swollen optic disc, but its use was so well established that attempts to abolish it were probably unrealistic.

Dr. S. P. MEADOWS said that raised intracranial pressure could not be ruled out merely because the optic nerve was not swollen. The degree of swelling varied even in cases of cerebellar tumour, which are particularly prone to early papillœdema. An unusual picture which Dr. Meadows showed was of papillœdema and retinal hæmorrhages in a patient with emphysema.

Mr. CHARLES COOK illustrated the histological changes in the swollen disc and showed how the retina in the immediate neighbourhood was shallowly detached. The course taken by the optic nerve-fibres in papillœdema, and the importance of the cul-de-sac of the subarachnoid space, were both demonstrated.

Treatment of Ocular Injuries

Mr. JOHN WHITWELL felt that the treatment of non-perforating injuries was almost as dull as refractions. He found little to choose between sulphacetamide (' Albucid ') and ' Polyfax ' (containing polymyxin B and bacitracin) as a routine ointment after the removal of corneal foreign bodies—the commonest of all injuries. Rust rings should be removed early. He pleaded for the admission of all cases of traumatic hyphæma, and for proper rest for all cases of considerable trauma, particularly in view of the danger of secondary hæmorrhage and glaucoma, which was very hard to treat and might lead to loss of useful vision or even of the eye. When glaucoma did ensue, the operation of choice was cyclodiathermy. Subconjunctival papaverine was suggested as a treatment for commotio retinæ. It was important to search the retina for tears even in the absence of retinal detachment.

Mr. M. J. ROPER-HALL, dealing with perforating wounds, said that recent improvement in the treatment of those wounds without retained foreign bodies was probably due to the meticulous suturing of the corneoscleral wounds, and the injection of air into the anterior chamber. Injection of air not only checked that the suture line was water (or air) tight but also discouraged anterior synechiæ. Conjunctival flaps had been almost abandoned. He recommended the use of magnification so that the surgeon could really see what he was doing—even for those surgeons who were not yet so presbyopic as to need reading glasses. Reposition of prolapsed iris, in very recent injuries, seemed to be justified in some cases. Mr. Roper-Hall felt that there was not so much hurry to remove intraocular foreign bodies that accurate localisation could be overlooked. It was better to wait if adequate X-ray or theatre facilities were not immediately available. He favoured the Mellinger-type magnet, especially for removal by the posterior route, which was usually the best method, unless the lens was much damaged already. Diathermy was not necessary to stop detachments after posterior removal, for the passage of the foreign body set up enough choroiditis to do that, but diathermy might reduce the risk of vitreous hæmorrhage. With non-magnetic foreign bodies it was justifiable to wait a week or two to gauge the strength of the ocular reaction since removal of these objects was likely to be very traumatic.

Mr. GILES ROMANES based his paper on the treatment of eye burns on cases treated at East Grinstead. When lid tissue had been lost, immediate action was necessary to cover the cornea, and he discussed the use of a bipedicle conjunctival flap and other possible methods. In chemical burns immediate and prolonged irrigation was the main essential.

Treatment of Retinal Detachment

In the Bowman lecture Prof. LOUIS PAUFIQUE (Lyons) surveyed the history of detachment surgery since the days of his youth, before Gonin had performed his first successful operation. He recalled that even in 1929 Professor Gayet had declared that " to wish to treat a retinal detachment one must be either a charlatan or a fool ".

Professor Paufique described the crude results with Gonin's thermocautery, then Weve's introduction of diathermy and his method of localising the retinal tears by transillumination. Then in 1950 came the operation of lamellar scleral resection to replace the more dangerous and difficult full-thickness resection of Muller and Lindner. Lamellar resection was elaborated, particularly by Shapland in England and Paufique himself in France, till it was now the operation of choice in about half the cases. Finally, Professor Paufique dwelt in some detail on the latest advances of vitreous transplantation (using powdered lyophilised vitreous) and light-coagulation. Evaluating his latest 524 cases, Professor Paufique recorded a 70% success-rate (a figure corresponding to most other recent assessments). Of the failures, in 15% the nature of the detachment could be said almost to have precluded a cure, but it was hard to explain why the other 15% failed.

Some other Subjects

Dr. ERIC LINNER (Göteborg, Sweden) assessed the rate of aqueous flow in disordered adrenal function, when the usual decrease at night was found to be significantly less.

Mr. A. G. CROSS described some cases of successful treatment of persistent vernal catarrh by the inlay of buccal mucous membrane.

Mr. W. E. S. BAIN described results with the recording tonometer recently introduced by Maurice, which allows the subject to move freely while wearing it.

Mr. L. G. FISON illustrated the difficulties in differential diagnosis of secondary retinal detachments, and the advantages of binocular ophthalmoscopy.

Mr. P. D. TREVOR-ROPER considered the evolution of visual artistry, attempting to bridge the gap that separates the non-representational " art " of birds and primates from the representational art of primitive man, in the light of the developmental stages of child art, near-blind painting, and blind sculpture.

Mr. F. C. RODGER described an investigation into the effect of citral and vitamin A on glaucoma, which had yielded rather indefinite results.

MANCHESTER MEDICAL SOCIETY AND LIVERPOOL MEDICAL INSTITUTION

Management of Thyroid Disorders

AT the annual joint meeting of the Liverpool Medical Institution and the Manchester Medical Society in Manchester on March 4, Dr. W. H. R. COOK opened a symposium on Current Trends in the Management of Thyroid Disorders.

After recalling that Prof. G. R. Murray was the first to treat successfully a patient with myxœdema, Dr. Cook dealt with recent work on myxœdema and Hashimoto's disease, and showed figures relating to fractionation of serum-proteins, liver-function tests, and precipitin tests carried out at the thyroid clinic of the David Lewis Northern Hospital, Liverpool, during the past two years. These findings agreed with the generally accepted views, but there was need for a more sensitive test than the precipitin test. He thought that the treatment of hyperthyroidism by anti-thyroid drugs should still be regarded as a preparation for surgery, which he preferred to the use of radioactive iodine.

After discussing the eye changes associated with the hyperthyroid state—namely, lid retraction, protrusion of the globe, œdematous changes, and extrinsic ocular muscle weakness or paralysis—Dr. Cook said that the corticosteroid hormones had a place in treatment of the œdematous changes. In 1955 a committee of the Medical Research Council reported unfavourably on the use of cortisone in exophthalmos, but it was notable that, of the cases recorded, all those in which chemosis was mentioned had shown a favourable result.

Mr. PHILIP HAWE discussed the results in a group of 1011 patients who had had thyroidectomies for all types of thyroid disturbance. He emphasised that many apparently simple goitres were malignant but could not be recognised as such on clinical grounds. Routine thyroidectomy on this account for cases of nodular goitre was impracticable, and he advocated a selective policy. There was an operative mortality of 0·2%, and the following morbidity figures were recorded: cord lesions, 2·4% temporary and 0·3% permanent; hypothyroidism 12%; recurrent thyrotoxicosis 2%; chronic tetany 0·2%.

Until the risk of carcinogenesis was definitely known, responsible physicians would continue to restrict the use of radioactive iodine, but it seemed the best treatment for primary thyrotoxicosis in patients over 45 years of age. In young patients with primary thyrotoxicosis, and in patients with toxic nodular goitre, Mr. Hawe thought surgery was preferable, the antithyroid drugs being used as a preparation for operation. Fluothane seemed likely to become the anæsthetic of choice. Pre- and post-operative laryngoscopies were already routine procedures, but direct laryngoscopy immediately before closing the wound had advantages. Routine preliminary exposure of the recurrent laryngeal nerve was practised throughout this series—a procedure which appeared to be increasing in popularity. The prevention of injury to the parathyroid glands remained the most difficult problem of thyroidectomy.

There was dissatisfaction with the present results of treatment of carcinoma of the thyroid, and Mr. Hawe advocated a more selective policy in choice of treatment and extent of operation. He questioned the wisdom of undertaking total thyroidectomy with a view to subsequent ^{131}I treatment. The fact that many thyroid carcinomas seemed to be hormone-dependent and could be controlled, for a time, by thyroid extract was encouraging.

Dr. W. KULKE discussed the investigation of thyroid function as an essential in the management of thyroid disorders. Referring to the use of radioactive iodine and the fallacies of interpretation, particularly with the two-hour thyroid uptake, he illustrated the value of the secretory part of the uptake curve, interpreted in association with plasma levels. While the diagnosis of hypothyroidism was not so effective, two tests, before and after T.S.H. administration, were useful in determining the origin of the hypofunction. As treatment of thyrotoxicosis by radioiodine was now so well established, it was prudent to consider the disadvantages and contraindications—the risk of carcinoma and leukæmia, the presence of pregnancy, the large goitre, the severely toxic goitre, and exophthalmos. Describing the value of radioiodine surveys in determining the uptake of a nodule, Dr. Kulke said that this investigation identified goitres suitable for ^{131}I therapy and indicated those likely to be carcinomatous.

Angina Independent of Effort

In a paper to the section of medicine of the Manchester Medical Society on March 25, Dr. K. SHIRLEY SMITH discussed recurrent angina independent of effort. After the first world war, realisation that pains below the left breast independent of effort need not be of cardiac origin, placed, by contrast, too much emphasis on the direct relation of angina pectoris to effort. He quoted instances of angina that were at no time evoked by effort yet in which the coronary causation was conclusively proven. There were two forms of postural angina—that connected with stooping and that related to recumbency. The recumbency angina might be an immediate consequence of lying down, or it might wake the patient after some hours' sleep.

Status anginosus was another (and the most severe) form of angina unrelated to effort. It was not necessarily a pre-mortal state, nor one invariably heralding cardiac infarction. Patients might survive several phases of status anginosus. Often this clinical condition corresponded to a certain type of cardiogram with ST depression in several leads, and on balance the evidence suggested that such patterns denoted subendocardial ischæmia. The cardiogram and the clinical state might evolve in one of several ways. Dr. Shirley Smith mentioned the phenomenon of linked angina, and emphasised the frequent coexistence and interplay of cardiac and non-cardiac syndromes.

Suturing of the Abdominal Wall

At a symposium on this subject held by the section of surgery on March 10, Mr. W. J. METCALFE compared the tensile strengths of upper abdominal midline and paramedian incisions in 16 pairs of rabbits on the 7th postoperative day. It was hard to compare clinical series because of variations in surgical techniques, and the age, weight, and disease of the patient. Each series of animals was made strictly comparable by using animals of the same weight, nutrition, and sex; the operative technique in the paramedian and midline series was exactly the same. A removable non-absorbable suture was used in each case so that no suture material contributed to the strength of wound at the time of testing. Using previously inserted traction sutures a distracting strain was applied to the wounds on the 7th postoperative day and the results read in volumes of water. A significantly greater volume of water was required to distract the midline than the paramedian wounds.

Reviews of Books

A Guide to Orthopædics

T. T. STAMM, M.B., F.R.C.S., orthopædic surgeon, Guy's Hospital, London. Oxford: Blackwell Scientific Publications. 1959. Pp. 115. 12*s*. 6*d*.

"ORTHOPÆDICS", says Mr. Stamm, "is usually regarded as being a difficult subject". Certainly the locomotor system is subject to an immense variety of injuries, degenerations, and diseases, so that the doctor who endeavours to diagnose them by reference to one of the comprehensive standard textbooks may be pardoned if he feels confused. But the great majority of patients at an orthopædic clinic have fairly stereotyped complaints, readily susceptible to clinical methods of investigation in the first instance, and to conservative treatment.

The value of this little book lies in the sensible restriction of its scope, and it is, in fact, a guide only to the commoner aspects of orthopædics. It deals with such recurrent matters as backache, minor foot troubles, and chronic arthritis, from the standpoint of the general practitioner, and shows how successfully he may serve his patients in a field which is not really, the author remarks, "a specialists' speciality" at all.

Medical Laboratory Investigations

IAN DAWSON, M.A., M.D., M.R.C.P., reader in pathology, University of London. WILLIAM GOLDIE, M.A., M.B., F.R.C.P., senior consultant in pathology, St. James's Hospital, Leeds. London: Butterworth. 1958. Pp. 260. 35*s*.

THE two authors are happily matched: one a reader in pathology and honorary consultant pathologist at a London teaching hospital; the other a senior consultant and part-time lecturer in pathology. In a foreword Prof. R. J. V. Pulvertaft points out that no doctor who qualified more than ten years ago received, as a student, basic instruction on many medical laboratory investigations and their interpretation which are now in daily use. No branch of medicine has expanded in scope and man-power so rapidly as clinical pathology. The difficulty facing many doctors is to decide what to ask of the laboratory, and they may also lack the experience to interpret the reports: this volume will be a great help to them. It tells the physician, the family doctor, and the hospital resident which laboratory investigations will be of real value, and there are detailed instructions on the completion of request forms, and the collection, packing, and dispatch of specimens. Normal values are given in an exhaustive table, and there is also an account of the errors of techniques.

The most attractive feature is the number of tables, which are a very quick aid in case of doubt. A table giving the findings in the cerebrospinal fluid in various diseases covers two pages. Another giving the common causes of leucocytosis is slightly larger and is subdivided into neutrophilia, eosinophilia, basophilia, lymphocytosis, and monocytosis. Sometimes the reader will be disappointed (if for example, he wants the normal value for protein-bound iodine in thyrotoxicosis, he is told that this technique is extremely difficult and few laboratories are prepared to undertake it; and similarly, this is all the information which he can obtain about measurement of radioactive-iodine uptake). Of the mercury content of urine, it is said that it is a test more popular with pædiatricians than with pathologists, and serum-cholinesterase level is said to be raised in liver disease.

This book answers a real need and is bound to become a very popular companion in the ward as well as in the study.

The Ecology of Human Disease

JACQUES M. MAY, M.D., director, medical geography department, American Geographical Society, New York. New York: M.D. Publications. 1959. Pp. 327. $7·50.

Charles Creighton was the last person who was able to write inclusively on the natural history of diseases. While he drew his material from thirteen centuries he confined it to Great Britain, and his refusal to admit that bacteria (or viruses) were the cause of infectious disease simplified his task enormously. More recently others far bolder have tried to cover the whole world, and the latest attempt confirms that global epidemiology is a labour beyond the strength of any one man. Dr. May's book is the first of three intended to describe the distribution of infectious and non-infectious diseases and the factors which determine it. After some chapters on theoretical background the author examines thirteen diseases on a standard plan. After defining the disease he discusses the infectious agent, the primary and secondary hosts, the circumstances which enhance or discourage infection, the geographical distribution, and the factors, inorganic, organic, and cultural, which have a bearing on this.

The author is a scholar, but the truth is that the task is now beyond any single person. Indeed it may be felt that the size of the book is about right for one on the geographical distribution of tuberculosis and the factors which influence it. Those on brucella or salmonella infections might easily be just as long. In no case would they be exhaustive, but they could usefully assemble the facts and theories now scattered through an impassable printed thicket.

A History of Cytology

ARTHUR HUGHES, M.A., PH.D., SC.D., lecturer in anatomy, University of Cambridge. London: Abelard-Schuman. 1959. Pp. 158. 21*s*.

OTHER than J. R. Baker's classical papers on the history of the cell theory and the opening chapters of Cameron's *The Cell*, there are no comprehensive histories of cytology in the English language. This book then is a welcome addition to the few scholarly works on the history of the biological sciences.

Dr. Hughes first shows how the development of cytology has largely depended on improvements in the instruments and methods used by cytologists—the microscope, staining and embedding methods, and the microtome. Many of these technical advances were outside the field of cytology and thus formed a major part of the environment which affected the progress of the subject. Of the internal factors—the origin and development of theories about cells—Hughes gives a fairly full account of the history of the cell theory; theories of cell formation; the importance of the role of the nucleus in theories of inheritance, and the history of the discovery of cytoplasmic structures. Finally, he discusses the importance of the cell theory in general biology, embryology, protozoology, genetics, &c.

It might have been better if the internal logic of the science —the objectives of cytologists, their approaches and evolving ideas—had not been so sharply separated from the influence of the external environment; in the shape of independent developments in other sciences. Further, little is said about the importance or otherwise of the social and philosophical background to the developing subject, or to the professional and institutional circumstances of cytologists.

The book is accurate and scholarly so far as it goes, but it is by no means the last word: it might have been called An Introduction to the History of Cytology.

Long Term Illness

Editor: MICHAEL G. WOHL, M.D., F.A.C.P., former clinical professor of medicine, Philadelphia General Hospital. Philadelphia and London: W. B. Saunders. 1959. Pp. 748. £5 19*s*.

LIKE many American textbooks, this is big, heavy, beautifully produced, and many-authored (79 contributors, under the general editorship of Professor Wohl). Its aim is to be "part of the sunshine of hope which has dispelled past gloom about prolonged illness". It is intended for "the practising physician who maintains an interest in the total care of the patient with prolonged illness".

The first part is concerned with principles of hospital and home care, and although it is sometimes diffuse it shows many ways in which handicapped patients can be helped to get the best they can from life. This section is particularly well illustrated. The second part is entitled Therapy of Specific Diseases, but consists in fact of a series of essays on the

ætiology, pathology, and treatment of a number of chronic diseases, and in some cases includes remarks about future prospects of treatment. Most of what is written here is up to date and in accord with modern belief. Some sections, such as that on drug addiction, refer to conditions peculiar to the United States.

Parts of this book are admirable, but it is hard to picture it finding many buyers in this country.

Treatment of Lung Cavities and Endobronchial Tuberculosis

BERYL E. BARSBY, M.D., M.R.C.P., chest specialist, Malaya. Edinburgh: E. & S. Livingstone. 1959. Pp. 147. 20*s*.

THIS book is partly a study of tuberculous cavities and bronchi by bronchoscopic, morbid anatomical, and radiological methods, and partly a record of the author's experience of treating tuberculosis under difficult conditions in Malaya. Looked at either as an original contribution to knowledge or as a manual of instruction for physicians working in similar circumstances it has something of value. The original work was painstaking and thoughtful and carried out " in the field " with little technical assistance: the advice is based on extensive experience and deserves attention. Interest in tuberculosis is declining in many of the more favoured countries; but there is still a great need for books such as this that record the application of sound fundamental principles of treatment in the less fortunate parts of the world.

Roxburgh's Common Skin Diseases (11th ed. London: H. K. Lewis. 1959. Pp. 215. 37*s*. 6*d*.)—" Roxburgh " is popular because it is well written and illustrated. This edition, revised by Dr. P. F. Borrie, preserves these virtues, although some of the old blocks seem to be getting worn and the coloured plates are not of the first order. The chapter on syphilis has been rewritten by Dr. C. S. Nicol, and there are many discreet alterations throughout the text, bringing it largely up to date. References to eczema are scattered about the book under the headings of eczema, dermatitis, seborrhœic dermatitis, &c., in a way that must confuse the beginner. Psychological factors receive little attention, though they are of much importance in the management of skin cases, whether ætiologically significant or not. Nevertheless, it remains a good book.

Mental Health Manual (London: British Red Cross Society. 1958. Pp. 86. 3*s*.).—Dr. David Stafford-Clark's ability to make psychiatric concepts clear and sensible, particularly to lay audiences, is very well known. In this booklet he has excelled himself: an ABC of personality development and the phases of life are followed by their application to the care of patients with organic and psychiatric illness, and to psychological first-aid after major disasters. The book is a joy to read and the Red Cross are to be congratulated on their sponsorship. Nurses and aids of all kinds should be encouraged to study it.

New Inventions

RESCUING A BROKEN NAIL

OCCASIONALLY a Smith Petersen nail breaks in the femoral neck. To remove the outer fragment is simple, but the inner fragment presents some difficulty. The instrument here illustrated has been devised at the Royal Northern Hospital to enable the deep fragment to be removed simply and without much damage to the bone.

The instrument is manufactured by Down Bros.

F. P. FITZGERALD
M.B. Dubl., F.R.C.S.I.

London, W.1

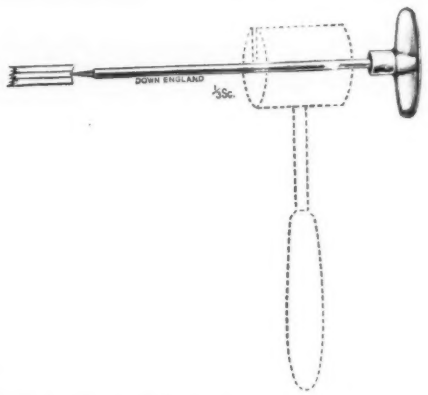

Fig. 1—A $^{1}/_{8}$ in. rod of steel with a right-angled handle and a tapered point. The tapered point is tapped so that it can enter the canal in the broken nail. It is introduced under X-ray control.

Fig. 2—The broken nail.

Fig. 3—Distal fragment has been removed. Tapered rod is being inserted into hole in nail. It is twisted until tight, and then removed by tapping handle with split mallet.

Fig. 4—After operation.

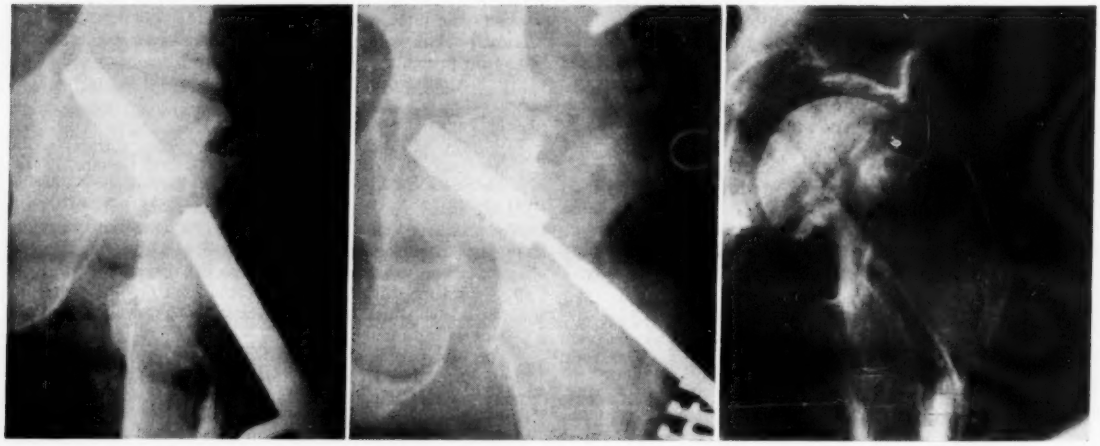

Fig. 2. **Fig. 3.** **Fig. 4.**

THE LANCET

LONDON 2 MAY 1959

Doctor and Factory

EVENTUALLY, said the Dale Committee eight years ago, there should be comprehensive provision for occupational health, covering not only industrial establishments (large and small) but also workers in shops and offices. One reason why so little has yet been done to this important end is that there are several different ways of doing it. Should the occupational health services come under the Factory Department (now part of the Ministry of Labour) or be an extension of the local public-health services under the Ministry of Health; or should the M.O.H. and H.M. medical inspector join forces in some way? And what part should be played by the general practitioner, as part-time works doctor or otherwise? Though these questions have been answered in various ways by people who see the need to get something done, no general policy has evolved, because nobody has accepted responsibility for seeing that "eventually" becomes "soon". The reason why we have given so much space to Lord TAYLOR's report, concluded in our present issue, is that we see no reason why the plan which works at Harlow should not work elsewhere. And, in its insistence that an occupational service should be primarily *clinical*, it breaks out of the old area of contention.

The truth probably is that in this long affair the real protagonists have been not so much the two Ministries as the two sides of industry—the employers and the trade-unions—and these two sides have much in common, though their exertions so far seem to have been directed rather to stopping what they regard as wrong than to promoting what they agree to be right. On the whole it seems that both employers and workers, for reasons which appear good to them, reject the idea that an industrial health service should be run by the M.O.H. and the local authorities. Because they dislike the thought of local-authority "interference" in industry, they oppose any scheme for a service under the ægis of the Ministry of Health. They nevertheless cooperate fully with the two other great sections of the National Health Service—the hospitals (especially their casualty and orthopædic departments) and the general practitioners, who, when off duty from the N.H.S., provide the great majority of the medical officers in industry. The trade-unions, for their part, favour an industrial health service under the ægis of the Ministry of Labour, with whose workings they are familiar; but this is a responsibility which the Ministry—admirably performing a law-enforcement function with a factory inspectorate which is microscopic in relation to its job—has shown singularly little wish to shoulder. The employers, naturally, do not relish the idea of an extension of the Factory Department permanently stationed in every large factory or group of factories, giving treatment and advice to all who need it at work, yet at the same time backed by police powers. Indeed it is hard to see how such a service could do real good, for either workers or employers. The doctor in the factory must be able to give advice to all as a friend, and his advice must be sought with as much confidence in professional secrecy as that of the family doctor or consultant. If it is to succeed, the industrial health service of the future must be divorced from police functions.

Faced with the need for health services, industry itself has taken time by the forelock and has developed services of its own; already in 1955 a review of 21,693 factories showed that 421 had whole-time doctors and 4195 part-time.[1] Employers then, are rapidly creating piecemeal an industrial health service, whether the Ministries like it or not. But, if industry is to pay for its own services, a major part in running them must be played by the employers in whose premises they operate, and by the trade-unions whose members are served. Where Lord TAYLOR feels that the official planners have gone wrong is in failing to make a job-analysis of the work to be done: they have been hypnotised by the word "prevention". What employers and workers need first of all, he believes, is a treatment service, to deal with the multitude of minor accidents and injuries which occur at work. (This, indeed, is what industry is already setting out to provide for itself.) They need also medical examinations, keyed into the work. Only when these two sides of the service have won general respect by their manifest efficiency can the third side, the prevention of industrial illness and accident, and the promotion of positive health, come into play. Management establishes a medical service because, in terms of working time saved, it is a paying proposition. Workers welcome such a service for the same reason—that they can get treatment at work without loss of time or wages. It is from this basis that the industrial medical officer can best win the position of adviser on hazards and working conditions and on the stresses and strains of management and labour relations.

On this view, industrial medicine has far more in common with the work of the general practitioner and of the regional board than of the local health authority; and this applies even on the side of industrial hygiene and toxicology. MCLAUGHLIN has described occupational or industrial medicine as "simply clinical medicine applied to industry",[2] and Lord TAYLOR [3] recently put the same thing in another way: "A large part of industrial medicine is neither more nor less than general practice conducted in the context of the factory or other work-place". He thinks that the primary tie-up between an occupational service and the N.H.S. should be with the local practitioners and with the casualty, orthopædic, physiotherapy, dermatological, and pathological departments at the hospitals.

The main difficulty in operational planning is to know how to meet the needs of the 230,000 small factories,

1. Annual Report of H.M. Chief Inspector of Factories for 1955.
2. McLaughlin, A. I. G. *Lancet*, 1953, ii, 105.
3. Taylor, S. *Practitioner*, 1958, **181**, 133.

and the building sites, shops and offices, and other workplaces in which more than half our workers are employed. To try to meet the needs of each individually is clearly fantastic. The answer must be the group occupational service, whether based on a special centre or a hospital. The essential desiderata of such a service are set out in detail by Lord TAYLOR as a result of his experience at Harlow. The Harlow pattern owes much to Dr. AUSTIN EAGGER's great experiment at Slough; but its scale is rather smaller, and it has the big advantage that (apart from five-elevenths of Lord TAYLOR's time) it has made no additional call on medical man-power. The pattern of organisation at Harlow is of special interest: control rests firmly on the employers, backed by the unions, with all branches of the National Health Service in the locality fully associated. Here seems to be an arrangement which might end the quarrels which have impeded progress. Of course a national service cannot be built in a day; but, judging by Harlow's experience, a comparatively small expenditure by the Government is all that is needed to enable industry to create its own group services on an increasing scale. If, on the other hand, this financial pump-priming is not forthcoming, relatively little will continue to happen.

Pregnancy Complications and the Child

THE mother's health in pregnancy is not generally thought, except in folk-lore, to be of any great importance in determining the after-development of her infant, unless she is grossly malnourished or suffers from an infection, such as rubella or syphilis, which passes the placental barrier. Otherwise the placenta seems to protect its charge from the fiercest of slings and arrows. Thus CREAMER [1] could discover no difference between 94 children of toxæmic pregnancies and 74 controls; and CARTER,[2] looking back over the histories of 219 pregnancies resulting in a malformed child, could find no relation to birth order, seasonal incidence, previous abortions, or maternal conditions in pregnancy. These observations, however, do not correspond to the findings of PASAMANICK et al. in the U.S.A., who have carried out carefully planned surveys over the past fifteen years in an attempt to throw light on ætiological factors operating in the prenatal period.

Interest seems to have been focused on the influence of maternal condition in pregnancy by earlier work on developmental differences between white and Negro children, which were found to be negligible—the slightly lower verbal responsiveness of the Negro toddlers was thought to be due to inhibition by the white examiner and the accelerated motor behaviour to a more permissive upbringing.[3 4] This contradiction of previous findings was thought to be related to the more adequate and standardised diets of mothers under war-time rationing. In subsequent work many cases of a certain disorder would be listed and the birth certificates of the infants obtained. The next registered birth matched by race, place of birth, and maternal age acted as control; and details of pregnancy and delivery were obtained either from the certificate itself (which seems to be a much fuller document in the U.S.A.) or from hospital case-records—home deliveries being eliminated in the latter studies. The results over the years have led PASAMANICK to postulate a "continuum of reproductive casualty" wherein severe effects lead to fatality (i.e., abortion or stillbirth); lesser ones to organic disease such as cerebral palsy, epilepsy, and mental defect; and milder still to "borderline" organic conditions such as behaviour disorder and tics. The maternal conditions which correlated most closely with disorders in the infants were those likely to lead to fœtal anoxia, such as antepartum hæmorrhage and placenta prævia, and the toxæmias. Dystocia seemed less important; and, oddly, operative procedures at birth did not correlate at all with disorders in the infant. The 561 cases of cerebral palsy studied in New York State gave the clearest relationship [5 6]; and 396 epileptics showed a similar pattern, the difference between the cases and controls being beyond the 5% level of significance.[7] Premature births were commoner among the propositi, and there was an association with maternal history of previous infant loss. (These relationships were much less clear in the non-white group of epileptics.) Similarly, behaviour disorders (1151 children) were significantly related to maternal disease; and where this association was found the offspring usually belonged to the "confused, disorganised and/or hyperactive group", which is often held to be organic.[8] Reading disorder [9] and tics [10] were less clearly but still positively related, but speech defects were not.[11]

The American workers are aware that these findings must be interpreted cautiously: retrospective data, although objective, may be biased, and postnatal influences were not studied. Perhaps some common factor underlay the tendency towards pregnancy complications and the later development of defects, or perhaps a complicated pregnancy may have led to a higher incidence of, say, gastroenteritis or encephalitis. Moreover, the 5% level of significance would not be accepted by all workers as high enough. On the other hand, the summation of the results of the various studies and the way in which the effect of maternal state is graded should not be lightly dismissed. But, however valid these findings, the number of cases associated or possibly "caused" in this way is a small minority of the total; and similarly most pregnancy complications are without harmful after-effect. In recognition of the need for careful longitudinal studies, 500 premature infants are being compared with 492 full-term controls: at 40 weeks a correlation between prematurity and serious neurological abnormality

1. Creamer, B. *J. Obstet. Gynæc. Brit. Emp.* 1955, **62**, 914.
2. Carter, C. O. *ibid.* 1950, **57**, 897.
3. Pasamanick, B. *J. Genet. Psychol.* 1946, **69**, 3.
4. Knobloch, H., Pasamanick, B. *ibid.* 1953, **83**, 137.
5. Lilienfeld, A. M., Parkhurst, E. *Amer. J. Hyg.* 1951, **53**, 262.
6. Lilienfeld, A. M., Pasamanick, B. *Amer. J. Obstet. Gynec.* 1955, **70**, 93.
7. Lilienfeld, A. M., Pasamanick, B. *J. Amer. med. Ass.* 1954, **155**, 719; *Neurology*, 1955, **5**, 77.
8. Pasamanick, B., Rogers, M. E., Lilienfeld, A. M. *Amer. J. Psychiat.* 1956, **112**, 613.
9. Kawi, A. A., Pasamanick, B. *J. Amer. med. Ass.* 1958, **166**, 1420.
10. Pasamanick, B., Kawi, A. *J. Pediat.* 1956, **48**, 596.
11. Pasamanick, B., Constantinou, F. K., Lilienfeld, A. M. *A.M.A. J. Dis. Child.* 1956, **91**, 113.

(8·2%; compared with 1·6% in the controls) was appearing but the relation with maternal complications was not elucidated.[12] To show a significant relationship in other disorders requires vast numbers: with regard to epilepsy, for example, only 1 child in about 200 will be expected to develop the disease, and the figures of LILIENFELD and PASAMANICK [7] suggest that perhaps 1 case of epilepsy in about 10 is associated with prenatal complications. Nevertheless we hope that the longitudinal studies in progress in this country will take account of this interesting work and of that by STOTT on the effects of shock, anxiety, distress, and illness in pregnancy.[13]

In their latest work PASAMANICK and his colleagues are studying further the nutritional aspects of early pregnancy. They have shown that mentally defective children are more likely to be born in the first three months of the year, and therefore to undergo the first three critical months of formative intrauterine life in the hot summer months. Assuming from their earlier work [3 4] that undernourishment of the mother might cause failure of development, they examined the records for the hottest summers and found the highest numbers of defectives following them—summer encephalitis and increased birth-rate in the lower social group were ruled out.[14] Pregnancy complications of the types previously shown to be harmful were commoner at the time of the winter births, and this was ascribed to the supposed lower protein intake during the previous hot weather.[15] Summer-born children weighed less, perhaps owing to the mother's sparser diet at this time.[15] ANDERSON et al.[16] in this country found a correlation between poor social circumstances and a high rate of fœtal death from malformation of the central nervous system, and they refer to other work implicating anoxia in early pregnancy. Professor PASAMANICK's work, however, seems to suggest that fairly minor deviations in health and nourishment during pregnancy play a more important part in determining fœtal disorders than has hitherto been believed, and we await with interest further results from his active department. Meanwhile in America these new ideas have been widely accepted and are finding a place in preventive psychiatry.[17]

Nevertheless this work as a whole is not yet fully convincing. The diet of the village woman in Bengal contains a fraction of the protein in the diet of the most heat-exhausted American; and yet such observations as have been made among the less well-nourished peoples have included no record of an especially large incidence of epilepsy, palsy, or mental defect. One possible explanation is that adverse conditions in pregnancy lead to disorder in the offspring only if a rare maternal constitutional factor is present. Among epileptics the absence of relation to dystocia and obstetric operations suggests that birth injury matters little; but we cannot neglect careful work showing that cerebral damage may result from difficult labour and postnatal infection.[18] In this sphere the network of factors—genetic, prenatal, postnatal, dietetic, climatic, and sociocultural—makes elucidation of any "cause" or series of causes a daunting task. It is, however, a task well worth pursuing.

Control of Aldosterone Secretion

CORTICOTROPHIN only slightly influences the secretion of aldosterone by the adrenal gland.[19–21] Observations on dogs [22 23] suggested that secretion was stimulated by a neurohormone from the brain; and evidence of such a hormone has been described by DAVIS [24] and DENTON.[25] Constriction of the inferior vena cava in dogs increases aldosterone secretion [26 27]; and DAVIS showed by cross-circulation experiments that, if the blood from a dog with such a caval constriction is passed through the adrenals of a normal dog, aldosterone secretion rises sharply and falls to normal again when the cross-circulation is stopped. Confirmatory evidence in sheep with adrenals transplanted into the neck has been reported by DENTON, though he measured changes in electrolytes in saliva and not aldosterone itself. Exactly where the neurohormone is produced is unknown. FARRELL [23] suggested that the posterior hypothalamus was the site, but DAVIS [28] reports that extensive destruction of the hypothalamus in dogs does not affect aldosterone secretion. Unfortunately, the technique used in FARRELL's laboratory is unlikely to reveal small changes in aldosterone secretion, because his control and experimental values come from different animals: his results [29] and those of MILLS et al.[27] reveal the extent of the variation from animal to animal. FARRELL has, however, recently reported that the neurohormone controlling aldosterone is concentrated in the region of the pineal and subcommissural body.[30]

As regards the afferent pathway, the studies of BARTTER et al.[31] have established that changes in intravascular volume influence aldosterone excretion. The increase in aldosterone secretion associated with salt restriction seems to be due to contraction of blood-volume. By contrast the depression of aldosterone excretion effected by infusions of hypertonic albumin results from vascular expansion; and the afferent pathway is suggested by the studies of MILLS, CASPER, and BARTTER [27] on dogs. They found that the increase in aldosterone secretion brought about by constriction of the inferior vena cava was terminated

12. Knobloch, H., Rider, R., Harper, P., Pasamanick, B. *J. Amer. med. Ass.* 1956, **161**, 581.
13. Stott, D. H. *Lancet*, 1957, i, 1006.
14. Knobloch, H., Pasamanick, B. *Amer. J. publ. Hlth*, 1958, **48**, 1201.
15. Pasamanick, B., Knobloch, H. *Obstet. Gynec.* 1958, **12**, 110.
16. Anderson, W. J. R., Baird, D., Thomson, A. M. *Lancet*, 1958, ii, 1304.
17. Lemkau, P. V. Basic Issues in Psychiatry. Springfield, Ill., 1959.
18. See Earle, K. M., Baldwin, M., Penfield, W. *Arch. Neurol. Psychiat.* 1953, **69**, 27. Malamud, N. *in* Temporal Lobe Epilepsy (edited by M. Baldwin and P. Bailey); p. 149. Springfield, Ill., 1958.
19. Luetscher, J. A., Axelrad, B. J. *J. clin. Endocrin. Metab.* 1954, **14**, 1086.
20. Farrell, F. L., Rauschkolb, A. B., Koletsky, S. *ibid.* 1955, **15**, 852.
21. Liddle, G. W., Duncan, L. E., Jr., Bartter, F. C. *Amer. J. Med.* 1956, **21**, 380.
22. Rauschkolb, E. W., Farrell, G. L. *J. clin. Endocrin. Metab.* 1956, **16**, 915.
23. Farrell, G. L. Abstracts of meeting of Endocrine Society, New York, 1957; p. 32.
24. Davis, J. O. *Rec. Prog. Horm. Res.* 1959, **15** (in the press).
25. Denton, D. A. Lecture, University College Hospital Medical School, Nov. 19, 1958.
26. Davis, J. O., Pechet, M. M., Ball, W. O., Goodkind, M. J. *J. clin. Invest.* 1957, **36**, 689.
27. Mills, I. H., Casper, A., Bartter, F. C. *Science*, 1958, **128**, 1140.
28. Davis, J. O., Ball, W. C. *Amer. J. Physiol.* 1958, **192**, 538.
29. Rosnagle, R. S., Farrell, G. L. *ibid.* 1956, **187**, 7.
30. Farrell, G. L. *Rec. Prog. Horm. Res.* **15** (in the press).
31. Bartter, F. C., Biglieri, E. G., Pronove, P., Delea, C. S. Aldosterone; p. 100. London, 1957.

by release of the constriction; but the increase persisted if the vagus nerves were sectioned in the neck before the cuff was released. Vagal section alone had no effect on aldosterone secretion, nor did it prevent the rise following caval constriction. Continuous tracings of arterial and venous pressures and hæmatocrit measurements showed that the hæmodynamic state reverted to normal whether the vagi were intact or not. These results are rather surprising because they suggest that withdrawal of the stimulus which leads to increased aldosterone secretion is not followed by decreased secretion of the hormone. Data on the mechanism causing the rise in aldosterone are reported by BARTTER, MILLS, et al.[32] They found that in dogs increased aldosterone secretion resulted from constriction by threads placed round the carotid arteries. For this effect to appear the amount of constriction (assessed by the pressure in an artery distal to the carotid sinus) need only be enough to reduce the pulse pressure by a few millimetres of mercury. Release of the constriction was not followed by a decrease in aldosterone—presumably because the receptors which signal a decrease in aldosterone, and whose pathway is the vagus, were not stimulated. When the carotid arteries were denervated, aldosterone secretion could not be increased either by constriction of the carotid arteries or by caval constriction. Secretion of aldosterone, therefore, is controlled by a rather unusual physiological mechanism, in that the stimulus of decreased baroceptor stimulation leads to increased aldosterone production but removal of the stimulus alone will not reduce secretion. For this there is a second mechanism, involving the vagus, though the site of the receptors is not definitely known—there is suggestive evidence that they lie in the right auricle.[33 34]

It would be interesting to know whether the mechanisms in the dog operate also in man. WAGNER et al.[35] have studied the aldosterone response to sodium restriction in patients with postural hypotension. Although these excreted aldosterone, in some no increase in secretion followed restriction of sodium intake. This might accord with the mechanism suggested by the work of MILLS et al.[27] and BARTTER et al.[32] if it were shown that the postural hypotension in these patients was due to a defect on the afferent side of the blood-pressure control. SHARPEY-SCHAFER [36] pointed out that in tabetics the response to the Valsalva manœuvre is abnormal, and the defect was on the afferent side because the patients' blood-pressure rose when they were asked to do mental arithmetic. Patients with postural hypotension in whom aldosterone secretion does not increase when sodium is restricted have been found to have the same type of Valsalva response as the tabetics, and by the mental-arithmetic test the defect was shown to be on the afferent side.[19] In contrast, one patient with severe postural hypotension responded to a low-salt diet by an increase in aldosterone excretion, even though the Valsalva response was abnormal. In her case mental arithmetic did not increase the blood-pressure; which suggested that the defect was on the efferent side.[37]

This discovery of the afferent mechanism in the control of aldosterone secretion is of great interest because of the clinical conditions in which aldosterone excretion is increased. These conditions include the nephrotic syndrome, hepatic cirrhosis with ascites, and some types of heart-failure. In the nephrotic syndrome it seems likely that the loss of fluid into the tissues decreases the intravascular volume and thereby stimulates aldosterone secretion. In cirrhosis with ascites, the exudation of fluid into the peritoneal cavity may similarly stimulate aldosterone secretion. In heart-failure the situation is not so easily understood. The work of WOLFF et al.[38] suggests that increased aldosterone excretion is commoner in right-sided than in left-sided heart-failure. Although in both there may be enhanced stimulation of the aldosterone "turn-on mechanism", since the blood-volume is not decreased it is difficult to see why in right-sided failure the "turn-off mechanism" via the vagus does not operate. Further work on patients with normal and diseased hearts may be expected to elucidate this problem and perhaps add something useful to the treatment of heart-failure.

32. Bartter, F. C., Mills, I. H., Biglieri, E. G., Delea, C. S. *Rec. Prog. Horm. Res.* **15** (in the press).
33. Bartter, F. C. *ibid.*
34. Anderson, C. H., McCally, M., Farrell, G. L. *Endocrinology*, 1959, **64**, 202.
35. Wagner, H., Biglieri, E. G., Bartter, F. C. Unpublished.
36. Sharpey-Schafer, E. P. *J. Physiol.* 1956, **134**, 1.
37. Gann, D., Mills, I. H., Bartter, F. C. Unpublished.
38. Wolff, H. P., Koczorek, K. R., Buchborn, E. Aldosterone; p. 193. London, 1957.

Annotations

THE DRUG BILL

"THERE is undoubtedly a considerable amount of wasteful expenditure on drugs in the General Medical Service attributable to imperfect prescribing." The Scottish Committee on Prescribing Costs, whose plain-spoken report is summarised on p. 936, has no doubt that money is being misspent on drugs prescribed by general practitioners (quite often with the encouragement of hospital doctors); and the report examines many of the proposals that have been made for reducing this item of expenditure on the National Health Service.

The Scottish committee enjoyed a considerable advantage over its English counterpart, whose views are presently to be made public, because its deliberations could cover the hospital and specialist as well as the general medical services and could take note of the impact of one on the other. There is no doubt that the drug bill has risen in recent years, even when account is taken of the fall in the value of the pound and other circumstantial changes. One difficulty is to decide how far this increased spending has been offset by economies in the use of hospital beds, less time off work, lower payments in sickness insurance, and so on. But if, as the committee maintain, there is *waste*, saving elsewhere is no excuse; and the recommendations in the Scottish report (and those to come, based on the English inquiry) must be the stimulus to renewed action.

Restrictive measures were not popular with Sir James Douglas and his colleagues, but they do recommend that all possible means short of prohibition should be used to discourage the prescribing of drugs in Cohen Committee

categories 5 and 6. Prescription charges, they believe, should be retained, but the report does not go very fully into the consequences of such charges. In the end the most effective steps towards economy would probably be the changes recommended in undergraduate and postgraduate education and in the supply of pharmaceutical information to doctors. Of more immediate influence would be the discouragement of " blunderbuss " therapy (" the very antithesis of current teaching ") and some restraint on the less responsible forms of advertising. But, as the Scottish report observes, it is largely the doctors' ignorance of costs that is at the root of the problem.

POLLUTED RIVERS

THE legislators who in 1876 gave local authorities some powers to control the pollution of rivers had reason to hope that they were preventing some of the more offensive evils of a simultaneous increase of population and industry. They had to make some exceptions to the general rule—all Parliaments do—and at that time to discharge sewage into the sea or tidal waters probably seemed harmless to their learned advisers. The sea is by definition boundless, and tidal waters are but an extension of the sea. Salt water is to common thinking " clean ", and so it is compared with the turbid, stinking waters of the Irwell or Aire. Lastly it was expected that the tidal currents would carry away all foulness without labour or cost.

Slowly and painfully we have learnt better. All coastal waters within a few miles of a major sewage outfall contain bacteria derived beyond doubt from the human bowel. The numbers are probably too small to do much harm, but undoubtedly the purifying effects of sea water have been overestimated. Tidal waters are in a far worse state. Most estuaries discharge their burden of filth into the open sea only slowly and intermittently. On their banks are far more people and far more water-closets than there were in 1876, and in many estuaries the volume of industrial effluent of varying toxicity at least equals that of the domestic sewage. To free these effluents from their harmful properties is often expensive, and this factor has led many firms to establish factories in places where they are free to discharge untreated effluents into tidal waters.

In 1951 a new Act made the control of pollution the responsibility of the newly created river boards and allowed these, subject to Ministerial approval, to extend their sway to the tidal reaches. At the moment the owners of sewage plants and factories along the lower Dee are uniting to oppose the attempt by the Dee and Clwyd River Board to establish a statutory standard of purity for the river below Chester.[1] A short view from the bridge at Queensferry would suggest that the board has a good case, but the arguments are more complex than those of æsthetics. Being fed by countless rivulets in the mountains, the volume of water in the Dee fluctuates extravagantly. In a rainy season it dilutes the noxious discharges sufficiently for salmon to ascend in numbers to satisfy the more skilled anglers. (Anadromous fish, besides tasting nice, are an excellent indicator of water pollution.) In times of drought, however, pollution reduces the oxygen level of the water to a lethal level, as the inhabitants of Chester saw with their own eyes not long ago. The basic trouble is that the annual flow of the river remains more or less constant (or even decreases slightly owing to abstraction upstream) while industry and its pollution increase every year. The argument against the river board is a weighty one but quite simple—expense.

1. *Manchester Guardian*, March 18, 1959.

It is a pity that to many the words " river board " suggest a group of selfish landowners devoted to salmon fishing and nothing else. The Act which gave these boards life makes it clear that they represent everyone who uses the rivers for work or play—the chairman of the waterworks committee and the miller as much as the canoeist. Within fairly strict limits it is the job of the board to say what can or cannot be done with an irreplaceable local and national asset. In a civilised community the effects of river pollution on the public health are negligible, but it must be remembered that the use of purified river water for drinking is on the increase and that certain forms of industrial pollution make this impossible. After several hundred years manufacturers have abandoned the historic plea that cheap labour is the foundation of national prosperity. The case for the cheap disposal of noxious effluents is not much better. Industry swallowed the pill—a larger one—many years ago when the Act of 1876 attempted to prevent the fouling of rivers above the tidal limits, and, despite the Cassandras of that day, the mills continued to turn. Some of the problems involved in the disposal of wastes without causing pollution are formidable, but if the atomic industry can do these things others can. Polluted water is water wasted, and this country can no longer afford such extravagance. We must hope that the inquiry by the Minister of Housing and Local Government into the project of the Dee and Clwyd River Board is conducted in an exploratory and temperate spirit: this is a serious problem, and we do not yet know all the answers.

SURGERY IN OLD AGE

Is a patient ever too old to have an operation? This question is asked less often than it used to be, for opinion has swung towards more energetic surgical treatment of the elderly. This shift has been prompted more by clinical impressions than by documented evidence, and for this reason we welcome a report from Denmark by Amdrup et al.,[1] who review ten years' experience in the surgery of patients over 70.

In a Copenhagen hospital the number of elderly patients treated in the surgical wards has more than doubled since 1946: twice as many old people are now being operated on, and the operative mortality has fallen. The Danes conclude that old age alone is hardly ever a contraindication to a necessary operation, and that if elective surgery is contemplated the sooner this is done the better, since delay often leads to complications and to an emergency operation under less favourable circumstances. This is particularly true of hernias and gall-bladder disease; gradual enlargement of the hernia and recurrent attacks of cholecystitis make eventual operation more difficult. The Danes recommend a bold approach to resection of neoplasms in the alimentary tract, and do not believe that the presence of metastases should preclude excision of carcinoma of the breast. The geriatrician who has to treat the patient with a fungating ulcer of the breast to whom surgery has been denied would certainly support this view.

One of the most difficult problems in the elderly is to know when to amputate an ischæmic limb. The Danes believe that this should be done sooner rather than later, on the grounds that after amputation the patient's general condition often improves, and he does not waste time languishing in bed awaiting improvement that is unlikely

1. Amdrup, E., Halkier, E., Køster, K. H., Sønder, P., Zachariae, F. *Danish med. Bull.* 1958, **5**, 248.

to occur. For the same reason early pinning of all fractured femurs is increasingly common, and the geriatrician lucky enough to be supported by an orthopædic colleague who is willing to adopt this policy knows how valuable it is.

The value of this more positive approach is borne out by the discharge-rate achieved by the Danish workers: some 80% of their patients were discharged to their own homes, and only a small minority had to go to wards for the chronic sick. This approach is likely to be increasingly adopted elsewhere.

AVERTING THE CRUSH SYNDROME

IN the 1914–18 war amputation of a severely wounded limb within about six hours after injury was regarded as a life-saving measure. Observations in that war [1] led to the development of a type of experiment which is still familiar—namely, crushing the limb of an animal in order to gain information about the reaction of the body to trauma. This method involves (*a*) crushing the limb, and (*b*) applying a ligature, clamp, or tourniquet. The animal is comparatively safe while the tourniquet is "on", but dies when it is removed. Dale and Laidlaw's [2] original study of "shock" suggested that the liberation of an histamine-like substance was responsible for the general effects, but this was apparently refuted by Blalock,[3] who found that the effects of trauma were due to blood-loss, and by O'Shaughnessy and Slome,[4] who demonstrated a neurogenic mechanism. Results and conclusions seemed to depend largely on the details of the experiment—notably the type and siting of the tourniquet, and the extent of crushing.

Bywaters and Beall [5] in the 1939–45 war found that in patients in whom a limb had been crushed by falling masonry renal failure and death sometimes ensued. This outcome was believed to be due to the liberation into the blood-stream of large amounts of muscle-breakdown products, such as potassium and myohæmoglobin. In the damaged nephrons myohæmoglobin was found as casts, and it was considered that these might be blocking the tubules. Prevention of the "crush syndrome" rested on early and adequate replacement of lost blood, intravenous infusion of saline solution to increase the glomerular filtration force, administration of caffeine to stimulate diuresis, and amputation of the affected limb.

Thompson and Campbell [6] now describe findings relevant both to the classical crush experiment and to the crush syndrome. In dogs they dissected the femoral vessels in the groin and applied a wire tourniquet round the leg under the vessels. With the wire drawn tight the leg was presumably isolated from the body save by these vessels; both artery and vein were divided and cannulated in such a way that the flow of blood could be continued or interrupted, or replaced by perfused dextran, the perfusate being collected from the femoral vein. In the experimental group of seven animals this perfusion or "wash-out" (75 ml. dextran at 100–120 mm. Hg for 20 minutes) was performed four hours after crush, during which the main vessels were clamped off; heparin was used to prevent intravascular clotting. In a control group the dextran wash-out was withheld. After perfusion the circulation was re-established. The degree of myoglobinuria, hæmoglobinuria, myoglobinæmia, and hæmoglobinæmia was measured two-hourly thereafter. The most significant differences between the experimental and control groups were in the degree of myoglobinæmia and hæmoglobinæmia in samples of blood taken from the femoral vein. For example, in the experimental group the mean plasma level of myoglobin was 0·9 mg. per 100 ml. at 2 hr., 2·8 mg. per 100 ml. at 4 hr., and 3·5 mg. per 100 ml. at 6 hr., compared with 16·2 mg., 27·1 mg., and 15·0 mg. in the control group. There were also appreciable differences between the groups in the degree of myoglobinuria and hæmoglobinuria.

No matter how tightly a tourniquet is applied, tissue-breakdown products can still enter the main system; intraosseous venography has defined the remarkable deep venous circulation which springs from the osseous tunnels in the region of the neck of the femur.[7] But the work of Thompson and Campbell does indicate that perfusion may be valuable in the crush syndrome. The interval between crush and perfusion (as between crush and amputation) must be brief if this measure is to be of use; and the old rubber tourniquet still has a place in prolonging the safe interval.

The perfusion "wash-out" may have a place in the management of other episodes where oliguria is liable to follow arterial damage—for example, removal of an embolus (whether by embolectomy or heparin), injury to the femoral or popliteal arteries in fracture cases, local concussion injury to the artery wall, and, rarely, arterial obstruction during an operation for varicose veins.[8] In lesions of the aorta—notably aneurysm—interruption of blood-flow to the limbs is necessary where artery grafting is performed. Prolonged ischæmia invites the complication of acute renal failure, which may more easily be averted by perfusion.

ROYAL SOCIETY OF HEALTH

THE annual congress of the Royal Society of Health has been held this week at Harrogate. In a presidential address on Monday, Lord Cohen of Birkenhead declared that successes in the control of disease in the past half-century rested on a tripod of endeavour—preventive and curative measures and research. These in turn depended on two relatively modern ideas. The first was that the body was essentially a machine that could be investigated by the methods and instruments of physics, chemistry, and biology. The second was the concept of the "cause of disease". Many specific and necessary causes had been discovered; but recently the emphasis had shifted to general contributory causes, often acting in concert, without which the specific cause might be almost or completely harmless.

In devising preventive measures, psychological factors must not be overlooked: there was a clear need for study of methods whereby the public could best be made to appreciate the value of such measures. Statutory powers prevented an individual from endangering the community; but he might ignore measures designed to promote his personal welfare: Lord Cohen cited the high proportion of eligible people not accepting welfare foods, the low acceptance-rate in the 15–25 age-group and in pregnant women of vaccination for poliomyelitis, and the growing death-rate from cancer of the lung: "There is the strongest statistical evidence to show that the more cigarettes a man smokes the more liable is he to develop cancer of the lung. . . . Should not the prudent man accept this and act upon it?"

1. Medical Research Committee report no. 25. H.M. Sationery Office, 1919.
2. Dale, H. H., Laidlaw, P. P. *J. Physiol.* 1918, **52**, 355.
3. Blalock, A. *Arch. Surg.* 1931, **22**, 598.
4. O'Shaughnessy, L., Slome, D. *Brit. J. Surg.* 1934, **22**, 589.
5. Bywaters, E. G. L., Beall, D. *Brit. med. J.* 1941, i, 427.
6. Thompson, W. W., Campbell, G. S. *Ann. Surg.* 1959, **149**, 235.
7. Harrison, M. H. M. Personal communication.
8. Bevan, P. G., Stammers, F. A. R., Green, S. H. *Brit. med. J.* 1956, i, 610.

Medical Education

A NEW CURRICULUM

Proposals for an African School

A NEW medical curriculum is outlined in the second report of the committee which is advising the University College of Rhodesia and Nyasaland on the creation of its new medical school.* The following are extracts from the report, which appears in the *Central African Journal of Medicine*, 1959, **5**, 3 (supplement).

Objectives for Africa

In thinking and talking about the shape of medical education in Rhodesia our discussions circled round three main issues. One was a belief that, because the pattern of medicine in Africa is determined by environment to a degree unknown nowadays in the United Kingdom, a change of emphasis in the teaching of the "scientific" side of medicine was required; and that though a sound training in pathology was vital, there should nevertheless be a bias in favour of epidemiological and environmental studies rather than towards pure laboratory work—appropriate as this may be for other countries. We also had in mind the particular need in a country to which European medicine would, for the most part, be new, for a proper understanding of the people's psychological attitude towards disease and treatment. The second, which would apply wherever the school was to be, was a desire to achieve as great a degree of integration as is possible—and sensible—between the various parts of the medical course. The kind of integration we have in mind would have to be deliberately planned; a gentle wish for cooperation between departments is not enough. If it were achieved it would also do much to further our third aim—a determination to reduce, if possible, the load of factual information under which the student flags, or at least to make it more tolerable by a weeding-out of the redundancies and irrelevancies, and by insisting only on those facts which are essential to the making of a good doctor.

Content of the Course

Entrance Requirements

Future medical students should have attained a certain standard in the General Certificate of Education examination. We hope that the college will be prepared, as are a few of the United Kingdom medical schools, to consider boys and girls who have not specialised in science in their last year or so at school. We believe that, at present and for some time to come, the great majority of medical students should be required to do their premedical course in the college.

Towards Integration of the Course

In the conventional pattern of medical education preclinical and clinical teaching are sharply separated (in certain medical schools in the United Kingdom one might even say segregated), and this separation is reinforced by the iron curtain of the second M.B. examination.

To avoid this unprofitable division it is proposed that instruction in anatomy and physiology (including psychology) should continue throughout the length of the course; conversely, the student should be brought into contact with patients early in his medical education. These proposals could be incorporated in a curriculum; but, to be effective, they must be the outcome of an attitude of mind which sees the need for instruction in pure and medical sciences to be relevant to medical thought and practice. Behind all our suggestions lies, quite simply, the contention that, throughout the whole of the course, where ideas and techniques can be as well taught on humans as on animals, in the wards as by textbooks, then choose the humans and the wards.

FIRST-YEAR (PREMEDICAL) COURSE

The general structure of the existing first-year medical course for 1st M.B. (or of the courses which confer exemption from 1st M.B.) has changed very little over the past 50 years. Even if it had been a superlatively good course when it was first devised, it could hardly be so now; and indeed it is not.

Zoology

The "type" system of teaching systematic zoology, introduced (it is said) by Rolleston in Oxford in the 'seventies, was all very well in the days when the concept of evolution, and therefore of the fundamental similarities of ground-plan between outwardly dissimilar animals, was still a novel and stirring concept.

Today one cannot but feel that the evolutionary panorama should be unfolded in a brisker and somewhat more peremptory way than hitherto. The lesson of evolution and of the general continuity and connectedness of animal forms can be taught without having more knowledge about hydra, the earthworm and the cockroach and the dogfish than can be written down on half a page for each. (It is sometimes rather faintly argued that practice in dissecting these "types" makes for good surgery, but we doubt if it does anything of the kind.) The same goes for much of the detailed special anatomy. The skeleton of the frog and the skull bones of the dog—usually taught without any consideration of mechanical fitness in the one case and without any consideration at all in the other—might likewise be pensioned off after their long service to the profession: there is too much else to do.

As to histology, if a student cannot study the histology of human (or other mammalian) thyroid gland without grasping that this organ is the counterpart of a structure which he had actually seen in the frog, then his powers of generalisation must be too feeble to justify his further education.

Botany

Very similar considerations apply to the teaching of botany.

A student will want some general conception of the plant kingdom, and there is a great deal of elementary cellular physiology which he must learn, and can in fact learn better on plants than on animals. The same is true of cellular anatomy and the organisation of simple tissues, and it is in the botany department that the future medical student might well be introduced to the use of the microscope. The detailed anatomy of the flowering plant, however, is knowledge which, we believe, the future doctor should be able to do without.

Such criticisms are far from new, and all astute teachers of biology have already gone as far to meet them as the existing formal syllabuses allow.

We have no intention of proposing that the teaching of matters of fact should be replaced by a teaching of "principles". The idea that principles can be taught abstractly is known to be an illusion by all those actively engaged in teaching. It is an illusion, too, that in biology any great body of principle is known. "Principles" are being groped after by those in the forefront of research; they are the last knowledge to be gained, and can hardly be the first to be imparted.

* The committee consists of Mr. LESLIE FARRER-BROWN, chairman, Prof. W. MELVILLE ARNOTT, Prof. T. H. DAVEY, Prof. A. D. M. GREENFIELD, Prof. P. B. MEDAWAR, Dr. HONOR SMITH, Prof. R. MILNES WALKER, and Miss GRACE MCDONALD (Secretary).

Finally, we believe that the course should have constant regard to the fact that those who study it will ultimately become doctors; if what must be learnt can be learnt as well upon medically relevant material as upon any other, then the former should be preferred.

Physics and Chemistry

A first-year (premedical) course must provide students with a good grounding in elementary physics and chemistry, with the course in chemistry leaning further towards physical chemistry than might be thought necessary at this stage for a future student of pure science.

We hope that the course in physics will make special concessions to students of mediocre mathematical ability, and that it will be illustrated wherever possible by examples or applications drawn from biology and medicine. Some reduction in systematic inorganic chemistry and qualitative inorganic analysis might make room for an expansion of physical and organic chemistry; and, in conjunction with the physics department, some mention might be made of the principles underlying the newer methods of quantitative analysis such as spectrophotometry and chromatography, methods of separation such as electrophoresis and paper chromatography, and the use of radioactive isotopes and labelled compounds. This is the stage, too, at which the student should be introduced to the elementary ideas of statistical mathematics—i.e., of variation, frequency distributions, sampling errors, and the comparison of sets of figures.

The Biological System

Some time should also be devoted to giving the student an understanding of the sociological or human-ecological situation in which he lives.

It is possible in seven or eight lectures for even an elementary student to grasp the meaning of life tables, fertility tables, age-distribution, morbidity-rates, and so on—and through the fairly intent study of these he may begin to grasp the shape of the forces that govern human mortality. From these the transition to elementary epidemiology as it concerns an African population would follow naturally, and so the student would come to a concept of social medicine generally; he cannot learn too soon that the health and welfare of man owe far more to hygiene, education, and mental attitude than to therapeutics.

Much use could be made of microbiology at the expense of part of the existing traditional course in botany. Micro-organisms provide real, but relatively simple, examples of growth, reproduction, elementary sexual processes (showing up very clearly the essential biological " meaning " of sexuality), variation, adaptation, population dynamics, and even evolution. Microbiology also lends itself to practical work that is not too difficult or elaborate for fairly large first-year classes. Rhodesia could set an example to the world in making the best use of the great resources of modern microbiology for elementary teaching.

We suggest that a good trial should be given to a properly integrated anatomical and physiological introduction to the teaching of organ systems. In this way the student might eventually get a *whole* conception, however elementary, of a working biological system, and it should eventually add up to a clear understanding of how the continued existence of the organism as a whole depends upon the mutual interaction of its parts.

Embryology and Genetics

Room must still be found for an elementary treatment of the earliest stages of development and of the evolution of developmental systems, for without this the embryology of man can be nothing more than a collection of pointless and inexplicable facts.

Genetics is one of the most difficult of elementary subjects to teach. Yet it is the one subject in biology with a comprehensive underlying theory, and some grasp of this theory is fundamental to any understanding of the biological situation of man.

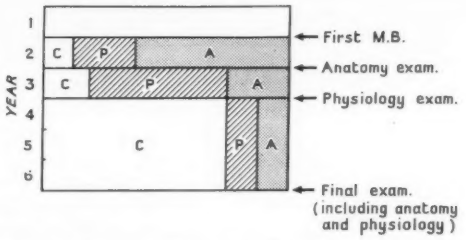

Diagram to illustrate the proposed 6-year medical course.
C=Clinical work and pathology; P=Physiology (including biochemistry and pharmacology); A=Anatomy.

SECOND AND THIRD (MEDICAL SCIENCES) YEARS

During this period of two academic years anatomy and physiology (including psychology) should occupy between them about five-sixths of the time, and clinical and pathological studies about one-sixth. If this suggestion were adopted the student's time might be allocated as shown in the accompanying diagram, the second year containing some physiology and the third some anatomy. At the time that histology is being taught, general physiology teaching should also be in progress so that the function of the parts is not presented out of context.

Not only would we like to see the teaching of anatomy and physiology coordinated in such a way that one subject would illuminate and amplify the other; we suggest that it would be most advantageous if, from the beginning of the medical sciences years, the student were given the opportunity of directly studying anatomical, physiological, and psychological problems as they are seen in the wards—if, that is, the rudiments of clinical medicine were dovetailed with his preclinical course. The aphasia that follows a stroke, the damage to memory that occurs with senile changes and in head injury are all good examples of conditions in which anatomist, physiologist, and psychologist, as well as the clinician, have a part to play.

If the teaching of structure and function are coordinated there is much to be said for an arrangement whereby students would be examined in anatomy at the end of the second year and in physiology (including psychology) at the end of the third.

Under such an arrangement the first examination would be predominantly anatomical but with some questions of a physiological kind. The second examination would be predominantly physiological but would include questions, not of a kind to test the candidate's detailed knowledge of anatomy, but to make sure that his comprehension of important structures is adequate. But whether the anatomy and physiology examinations are separated, or whether they are held together at the end of the third year, clinical teachers should be coexaminers, responsible for part of the examinations. Similarly the medical sciences teachers should be coexaminers on the same kind of basis in the final examinations.

Anatomy

The teaching of anatomy would gain by an arrangement whereby the main systems of the body were fairly rapidly dissected in turn on separate bodies; for example, dissection of the circulatory system would start at the heart and follow the main vessels to the periphery without troubling too much about relationships with other structure. Knowledge of relationships would come later, with dissection

of the other systems. The two outstanding advantages which would follow such an approach would be (1) that emphasis would be laid on important structures rather than minutiæ; and (2) that the dissections would co-ordinate very naturally and easily with histology, with the introduction to physiology and with clinical demonstrations.

One might hesitate to suggest such an approach in the case of a country with a very limited supply of material, but a Rhodesian school is not likely to be so hampered. Dissection of the whole body should be undertaken, but emphasis should be laid on, and a detailed knowledge required of, only those regions which are at present of practical importance. For example:

1. In the limbs, it is *not* necessary, except in the hand, to have a *detailed* knowledge of exact origins and insertions of muscles. It *is* important to know the innervations and actions of muscle groups.

2. It is *not* necessary to remember all the small arterial branches and the details of anastomotic channels. It *is* necessary to be able to follow the arterial system by surface palpation on the living subject and to know the consequences of interrupting the arterial system in various places for various times.

3. It is *not* necessary to remember (*a*) all the articulations of all the bones of the wrist; (*b*) the anatomy of the individual bones of the skull; (*c*) the exact date of calcification of bones and fusion of the various calcified centres.

Physiology

The main emphasis in the practical classes should be on human physiology and test of normal function, and much of the practical work on normal physiology could be done by students on each other. The layout of the physiological laboratory should therefore be such as to allow for the examination of one student, in a recumbent position, by another, while at the same time providing adequate room for bench space and circulation. Clinical cases with impaired function might occasionally be demonstrated to illustrate the size of the functional reserve in health and the consequences of its reduction. But, while emphasising human physiology, it will be most important to retain the classical experiments on isolated surviving tissues which demonstrate their properties, indicate the primary actions of drugs, and develop a proper respect for the delicacy of living matter. It will also be important to demonstrate a number of classical experiments on whole animals.

Rudiments of Clinical Method

The observations the clinical student must learn to make are derived from the patient's history and the physical examination. What the experimental method and procedure are to the laboratory-worker, history-taking and physical examination are to the clinician. For this reason the student should be taught at least the rudiments of clinical methods from the time he first meets a patient—that is (if our suggestions are adopted) from the beginning of the second year. A little later the student should learn that the limits to observation imposed by his five senses may be extended by special aids, and that, just as he can hear better and more conveniently with a stethoscope than with his naked ear, so his perception can be enhanced by the proper use of the ophthalmoscope, microscope, X-ray apparatus, and the special techniques of the bacteriologist and biochemist.

CLINICAL YEARS

If some of our suggestions for the first three years of the course might be described by those who like them as forward-looking, and by those who don't as breaking with tradition, our proposals for the clinical years cannot be said to follow other than well-tried and proven lines. Active clerkship on patients should be the essence of this period; as an educational method it is dependent for its success almost entirely upon the quality of the teachers, but if the teachers are good it cannot be bettered.

Nursing

In the early stages of the clinical course students should spend, say, a fortnight acting as nurses in the wards. The idea is not new; it is the practice in at least one English medical school where it has amply proved its value. In the Federation, where a doctor may have to practise without any skilled nursing help, even so brief an introduction as we propose to the tasks which a good nurse performs in caring for her patients would be still more of an asset.

Pathology

Pathology should be viewed as an integral part of clinical practice and not, in any way, as a laboratory service. Clinical pathology, on which there should be a strong emphasis—more so than in most schools in the United Kingdom—should be taught as an extension of the physical examination of the patient, the student learning not to be content with what his nose, his eyes, and his hands tell him. The student should be taught to do as much as possible of the investigation himself, helping in the routine tests, taking an interest in the whole patient (alive or dead), preparing notes under his tutor's guidance, and keeping a journal of his work.

It should be usual for lectures on pathology to be illustrated by fresh autopsy or biopsy specimens, current laboratory reports, &c., and we certainly hope that a new school may not feel any call to revert to the declining and sterile tradition of the pathology museum—the bottled specimens, the fading slides, so reminiscent of the gun-room with its mounted trophies. Rich though the tradition may be in racy tales of heroic and sanguinary episodes on kitchen table or in a rondevaal in the bush, it is of limited educational value.

There might well also emerge a sort of "diagnostic kit" which, for its versatility and portability, would represent the ultimate in field medical practice; this is the kind of arrangement Africa needs, where the aim must be "every doctor his own pathologist". The ideal would be for each student to own his microscope, and he should be helped to develop maximum efficiency with the simplest and least expensive drugs as well as portable intravenous kits, and efficient blood-transfusion apparatus organised on a "bush-proof" basis. To this end it would be an advantage if the head of the pharmacology department (whether it be attached to physiology or medicine) were a clinician, or at least a medical graduate with substantial clinical experience.

Medicine and Surgery

In so far as the training of students is concerned, we hope for a close liaison amounting almost to fusion between the departments of medicine and surgery. The most important aspect of surgery, in the education of a doctor, is the appreciation of the fact that surgery is not a separate discipline but that it deals with patients as individuals, and not just with their diseases or injuries. In many diseases there is no clear line of distinction between "medicine" and "surgery", and an operation is one incident in a course of treatment. To help to bring about the integration of medical and surgical teaching there

should be at least two wards (one male and one female) in which both the professors have charge of beds.

Many of the patients in these wards would be suffering from conditions of concern to both physicians and surgeons, but the main purpose of the arrangement would be to emphasise that there is no sharp line of distinction between the two methods of treatment.

The clinical lecture should be the normal, and some of these lectures, or lecture-demonstrations, occupying perhaps one or two hours on four or five days a week, would be of a wider kind, embracing all relevant facets of clinical practice, including applied anatomy and physiology as well as the many aspects of pathology, medicine, and surgery. Social medicine and psychiatry, the principles of which should permeate all clinical practice, would have a particularly important role to play in such lectures, and all students, irrespective of where they are clerking, should normally be required to attend.

A strong case can be made out for allocating each student to an individual tutor of registrar status, and for students keeping the case-notes—the responsibility for making sure that they are dependable falling on the registrars and housemen. Ward rounds should, in any case, be expositions by the clerks of their cases, annotated and illustrated by the physician or surgeon, rather than a monologue, however brilliant, in which the teacher asks numerous shrewd questions and answers them all to his own complete satisfaction.

Local Conditions

Under the general heading of medicine and surgery there are four points to which Rhodesia, because of local conditions, should give special attention.

1. In the Central African Federation where, except in the few larger centres, any doctor may be called upon to perform an emergency operation, the student's training should be such that when he qualifies he is well acquainted with the urgent treatment of all forms of trauma, and particularly of fractures, and is also able to carry out the more common emergency major operations.

2. All students should be fully conversant with minor injuries; thus a liberal amount of time during their surgical training should be spent in outpatient and casualty departments.

3. Eye diseases are common in Africa and a great deal can be done by preventive measures and by early treatment to prevent blindness. In planning the medical course, enough attention should be directed to ophthalmology. This is the one exception to our general view that, for the present, specialisation in the various branches of surgery can have little place in the undergraduate curriculum.

4. Nearly half the patients in African hospitals are children; in rural African populations nearly half the children die under six years of age. These two facts alone sufficiently underline the need for the study of pædiatrics to be accorded a substantial share in the medical curriculum.

Social Medicine

The aim should be to inculcate a way of thought in which the student would no more think of omitting to mention the diet, district, and "life situation" of the patient, than to deal with the temperature, pulse, and urine. It is in this context that we would like to see Rhodesia try out a village family scheme, following the example, though not necessarily the pattern, of the training given to students at Durban by the department of social, preventive, and family medicine, or at Vellore under its village health advisory service.

Psychiatry

Part of the student's education in psychiatry should be gained from clerking in psychiatric wards or on suitable cases in the medical wards. It is not necessary to have a large number of cases, but it is an immense advantage if the experience of psychiatric conditions which the student will gain in the outpatient department can be illuminated and placed on a surer basis by bedside teaching in the ward.

Obstetrics and Gynæcology

In coupling together obstetrics and gynæcology we bow to current practice. Yet there is much to be said for regarding diseases of women as best dealt with in the medical and surgical wards, and we certainly hope that gynæcology will be taught in a proper relationship to medicine and surgery.

It is most important for the young doctor whose practice is likely to be in Africa to be thoroughly competent in obstetrics. If, during his medical sciences years the student has been introduced to normal pregnancy in the antenatal clinic and to normal deliveries and postnatal care, he should have gained some background of knowledge by the time he starts clerking in the obstetric wards and with the wealth of material—both normal and abnormal—to be expected in the Harare hospital and in the surrounding districts, he should be able in the period (i.e., six months, of which two would be resident) to gain a wider knowledge and considerably more practical experience than his British counterpart.

Teacher and Taught

In the selection of staff the choice should fall, as a rule, on physicians and surgeons with a broad clinical background and an appreciation of patients as members of a community. It may even be thought that there is little place in a new medical school in the Central African Federation for clinicians who are advancing knowledge in a very narrow field and who devote most of their time to this field. We agree with this view provided that it is reconcilable, in an age of specialisation, with the need for the school to establish first-class standards of practice.

In Africa one sees too often a hopeless prognosis casually given. The doctor will say that that is the best that can be done in the circumstances though he knows well that in another place and with other resources, a great fight would be put up before defeat was admitted. This is a sad but not a wicked state of affairs: what, in our view, would be wicked, would be to allow a student to regard as satisfactory a standard of care that is less than first-rate in the present state of medical knowledge. It is to guard against this kind of possibility that we believe that, even in a new school, there is room for a quite high degree of specialisation, but from which the sting of over-specialisation has been removed by teamwork.

Self-reliance

It may be thought that a scheme of teaching based upon the sense of participation rather than the relationship of master and pupil is all very well in a country with a long and solid academic foundation, but the worst possible thing in a country in which a student has a very particular psychological dependence on the authority of teachers and the correctness of the written word. Yet this kind of dependence (so often found in students from countries where higher education is still something new) is perhaps one of the very first things that one should seek to undermine. Half the battle of education will be won if the student can come to rely upon and cultivate his own resources, and can be brought to believe that education is not something to be done to him but something he himself must do.

Special Articles

HARLOW INDUSTRIAL HEALTH SERVICE

Lessons of an Experiment in Industrial Cooperation

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MEDICAL DIRECTOR OF THE SERVICE

(*Concluded from p. 880*)

The growth of the service is shown in table III.

TABLE III—GROWTH OF THE HARLOW INDUSTRIAL HEALTH SERVICE

—	Attendances			Member firms (number of employees)			
	At centre	In factories	Total	Number of firms	With own nurse in factory	Without nurse	Total
1955–56							
First quarter..	1017	492	1509	13	2441	515	2956
Second quarter	1210	639	1849	18	2463	1310	3773
Third quarter	1289	1829	3118	21	2063	1748	3811
Fourth quarter	1322	1749	3071	23	2159	1982	4141
1956–57							
First quarter..	1369	1467	2836	26	2156	2099	4255
Second quarter	1490	1342	2832	27	2444	2210	4654
Third quarter	1778	1562	3340	30	2498	2335	4833
Fourth quarter	2028	1541	3569	30	2598	2411	5009
1957–58							
First quarter..	1920	1392	3312	31	2884	2450	5334
Second quarter	1634	1511	3145	32	2944	2510	5454
Third quarter	1823	1485	3308	37	3237	2550	5797
Fourth quarter	1938	1723	3661	40	3360	2622	5982

The potential cover is about 8100 workers; so the service is now meeting the needs of nearly three-quarters of its potential.

The sudden jump in factory attendances in the third quarter of 1955–56 was due to the takeover of a factory surgery from a full-time nursing orderly; this change is also reflected in the fifth and sixth columns. The attendances at this surgery subsequently fell to a figure which has remained stable for the past two years. There have been no complaints from the workers, and the management are satisfied that there has been a real saving in production time.

The level of treatment is up to that carried out in good general practice. Thus, skin suture under local anæsthetic is done in the clean surgery, but cases needing tendon suture are always referred to hospital. Similarly, all suspected wrist, ankle, and long-bone fractures are referred direct to hospital, only those of the metacarpals, metatarsals, and phalanges being dealt with at the centre. A trolley set up for minor surgery at night is always left in readiness, and an eye trolley and eye chair are available in the main surgery. Portable and static oxygen cylinders are available for the treatment of gas casualties, and there is a Riley rocking-stretcher for artificial respiration.

Orthopædic and *dermatological* clinics are held once a month. These will be increased when demand justifies it.

A weekly *ophthalmic* clinic has been in operation for a year. The ophthalmologist has a dispensing optician in attendance, but patients are free to get glasses dispensed elsewhere if they wish.

A twice-weekly *chiropody* clinic is held after working hours; for this, patients pay a charge of 5*s*. per treatment.

From the outset, simple *physiotherapy*, mainly infra-red treatment, has been provided by the nursing staff. With the opening of the hut extension, it has been possible to arrange for the regional hospital board to supply a trained physiotherapist. There are now two massage couches, five cubicles, short-wave diathermy, infra-red and ultraviolet lamps, wax baths, faradism, galvanism, sinusoidal treatment, and wall-bars. At present, there are three sessions a week, one being open to "non-industrial" patients from the town as a whole. It is a six-mile journey to the local hospital at Epping, and most of the patients treated are referred from the hospital outpatient clinics. Thus the burden on the hospital physiotherapy department is relieved, many working hours saved, and much travel avoided. A careful watch is kept to make sure that physiotherapy is given only when really necessary, to avoid the possibility of its exploitation for work-dodging.

The policy on medical examination of entrants to industry agreed by the visiting medical officers is as follows:

If a firm wishes to have all entrants examined this will be done. More usually, the request is that staff only should be examined before entry into a pension scheme. We do not think that universal examination before employment is essential, provided the officer engaging new entrants makes certain simple relevant inquiries. We do think, however, that workers in certain types of job, for example lorry, truck, and crane drivers, and foundrymen and chemical operatives, should always be examined, and periodically re-examined, for the safety of themselves and others.

This takes no account of statutory examinations by the appointed factory doctor. Our senior visiting medical officer is the appointed factory doctor for the area. He carries out his examinations at the centre, but in his own time.

A scheme for the voluntary regular health examination of higher executives has recently been started, and a visiting physician appointed. Each examination takes from one and a half to two hours, and a charge of £2 2s. per examination is made to the participating firm. So far, eighteen member firms are availing themselves of this facility.

In considering any further extension of the diagnostic and treatment facilities of the service, we have to be careful to avoid duplicating the proper functions of the hospital and specialist services and of the general practitioners. In so far as we provide similar cover, as a special service to industry, there must be proper coordination. This is best achieved by the industrial health service itself making use of specialists with hospital appointments and general practitioners.

At the same time, we have to remember that our first aim must always be the maintenance and restoration of the workers' health, with a minimum loss of working time.

Particular Problems

First-aid

Much attention has been given to the training of industrial first-aid workers.

In industry the provision of first-aid boxes is a legal necessity and almost all injuries are seen, in the first instance, by first-aiders; in practice, their work is largely confined to the treatment of minor trauma, and true first-aid for major emergencies. Accordingly, first-aid equipment has been adapted to meet their needs, and a training scheme evolved on the basis of job-analysis. Methods taught have to be such that they can be used without running water, as this is seldom available at first-aid points. Stress is placed on teaching the first-aider to do simple work really well, and to know when to send for help. A training manual, for use at our evening lecture-demonstrations, has been prepared. As a result of these measures, sepsis in minor injuries has been virtually eliminated.

Health Cover for the Building Industry

The biggest single industry in Harlow is the building trade; it is also the industry with the second-highest casualty-rate in the country. About one-tenth of all workers treated at the industrial health centre are build-

ing operatives. Much thought has been devoted to the recruitment of building contractors as members of the service.

The primary difficulty is that a per-capita membership is inappropriate, because many if not most of the workers on any building site are employed not by the main contractors but by subcontractors.

Accordingly, in cooperation with the building trade, a scheme has been worked out whereby building firms can become associate members of the service on two alternative subscription bases:

(*a*) One shilling per £100 value of the contracts covered, spread over the duration of the contract, and payable quarterly. Thus, a firm building, say, a £200,000 factory over two years will pay £100 in all or £12 10*s*. per quarter.

(*b*) £1 per week per building site covered.

Broadly speaking, (*a*) is best for smaller firms, while (*b*) is best for larger firms with contracts running into several hundred thousand pounds. It is calculated that either rate will cover expenditure.

For their subscriptions, building firms receive the full facilities available at the Industrial Health Centre, emergency cover on sites, training of first-aiders, and regular visits to each site by a trained industrial nurse, to see conditions and to stock first-aid boxes, on similar lines to our visits to factories. This is the more important, because first-aid on building sites is simple and often primitive.

So far six contracting firms have joined the service, and both management and workers express their appreciation.

The Distributive Trades

Rather more than half the working population of Britain is employed outside factories. Many transport workers and all mine workers already have industrial health cover. But most workers in shops and offices have no special health care at work. Traumatic risks are low, with certain exceptions such as the meat trade. There are, however, special problems wherever food is handled; and pyschological problems related to occupation abound. Primarily, their solution is one for management; but the experienced industrial medical officer can often give advice of real value to both sides.

So far, one large firm of multiple grocers, employing 40 people, has joined the service, on the same subscription basis as the factories. The shop is visited weekly and when necessary by a nurse, and weekly by a visiting medical officer. He works in full cooperation with the firm's own headquarters medical department. In the absence of dramatic traumatic risk, the extension of this side of our work is likely to be rather slow. Nevertheless, we believe something of practical value is already evolving.

Further Industrial Cover

We still have to increase our industrial cover.

In particular, there are four substantial wood-working firms who are non-members. They have considerable traumatic risks; but they are subject also to a risk of another kind. Any trade recession hits early and hard the makers of furniture and radio and television cabinets. In consequence, they are somewhat reluctant to commit themselves to the additional overhead, small though it is, which membership entails. We continue to treat their emergencies, and trust that in due course they will become members.

The Second Industrial Estate

Harlow's second industrial estate, called Pinnacles, is now under development (fig. 6). The factories on this estate are almost all of medium size with their own first-aid departments. We have therefore developed mobile nursing and medical cover as a first stage. This is now easy to achieve, because a fast motor road, Elizabeth Way, brings the two estates within five to seven minutes of each other by car.

The growth of the estate has been such that a second centre is now becoming urgently necessary. It is expected that this second centre will be something between Edinburgh House (without the extension) and the original hut. It will have ultimately to meet the needs of 7000 workers, and must have its own nursing and visiting medical staff. Its planning will give scope for further experiment in the economical provision of industrial medical facilities.

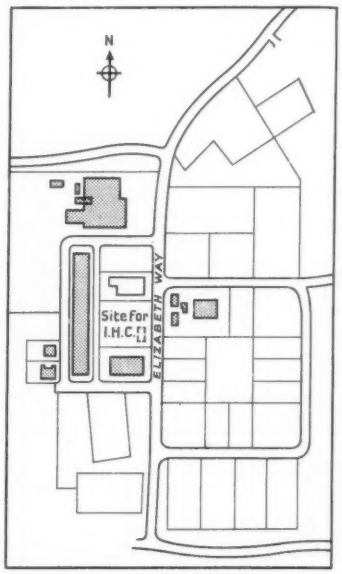


Fig. 6—Layout of Pinnacles (Western) industrial estate at Harlow, showing site for industrial health centre. Shaded factories are members of the industrial health service.

Lessons of First Three Years

1. Large factories usually provide their own industrial health service. For simple economic reasons, many medium-sized and almost all small factories find this beyond them. Moreover, the nurse in the medium-sized factory will often be underemployed, and may fill her time with clerical or other duties. Thus her nursing skill will in time decline. There are, then, medical as well as economic reasons against the multiplication of continuously staffed medical departments in medium and small factories.

2. Wherever a number of factories are grouped within a radius of say, one to two miles, a cooperative industrial health service can offer more comprehensive facilities than any individual factory could provide for itself for the same expenditure. Such a service must have a physical base for operations, where the main facilities for treatment are available. In some places, such a base might be linked with a hospital casualty department,[12] but in most industrial areas geography will necessitate the provision of an ad-hoc industrial health centre.

3. The first requirement from such a service is the speedy and efficient treatment of accidents and illnesses occurring at work, with a minimum loss of working time. Only when this provision has won the confidence of management and workers will advice on prevention and positive health be acceptable.

4. Mobility of nursing staff and doctors is essential from the start. Treatment of minor injuries and ailments in the factory itself is the ideal to be aimed at whenever possible. The training of first-aiders and the equipment and regular inspection and stocking of first-aid boxes and first-aid rooms is of great importance.

5. The quality of the industrial nursing staff will be a major factor in deciding the success or failure of the service.

12. Dr. T. O. Garland is at present operating such an experimental service at the Central Middlesex Hospital.

The industrial nurse has to take personal responsibility for most of her acts of service, without direct medical supervision. She must know precisely the limits of her own competence and when to get medical help. She must be kindly yet firm in her relations with both workers and management. She must not be underemployed. At Harlow, we have been most fortunate in the nursing sisters who provide the backbone of our treatment service. Moreover, they are actively interested in prevention, and their observations can often guide visiting medical officers to the points of excessive hazard.

6. The planning and initiation of a cooperative industrial health service is a major administrative task, not lightly to be undertaken. In its early years, such a service cannot hope to be self-supporting. At Harlow, we have yet to demonstrate that this can be achieved in due course.

7. The conception of a non-profit-making company, on the lines of the Slough Industrial Health Service, has been found to be a good one. Though the council should be widely representative, the proportion of management must be substantial since in the long run management is paying for it.

8. In areas where general practitioners are in group practice, there are substantial advantages in using them to provide the main medical cover. Medical care in industry has much in common with good general practice; but to the skills of the good general practitioner must be added a genuine interest in the working environment. By using general practitioners, such services can be created with a minimum drain on the available medical man-power. The only substantial disadvantage of employing general practitioners is that the administration is considerably more complicated.

9. In any cooperative industrial health service, a great deal depends on the medical director and the secretary-administrator.

They must be able to deal, on equal and friendly terms, with directors, consultants, general practitioners, trade unions, and officers of the many health authorities in the area. They must be technically and administratively efficient. The medical director must be ready to study and advise on the health hazards of industry, including industrial toxicology. The secretary-administrator must be able to undertake all ordinary aspects of personnel management, as well as book-keeping, paying of wages and salaries, the elements of company law and minute-writing.

At Harlow, for special reasons, both the medical director and the secretary-administrator are half-time only. Elsewhere, experience will show whether or not more time than this is needed to give the service required. The medical director is graded as a consultant on five sessions and the secretary-administrator as a half-time hospital secretary.

10. Experience at Harlow shows that to launch an efficient and comprehensive industrial health service a firm financial springboard is essential. Long term, we consider that our subscription-rates are satisfactory. But the build-up is bound to be slow. During this period, substantial financial help is necessary. Apart from buildings, the Harlow Industrial Health Service has received from the Nuffield Provincial Hospitals Trust the equivalent of £20,000.[13] This has so far proved just enough to see us through; but for some time to come a donation as well as a subscription income will be needed. In addition, capital expenditure by the Trust has amounted to close on £20,000, though the larger part of this is revenue-yielding in terms of rent. This does not include the cost of the second smaller centre on the Pinnacles estate.

13. Grant £18,000; initial salaries and costs before formation of service: £2000.

Assuming that the Harlow Industrial Health Service will ultimately look after 15,000 workers, the initial capital expenditure will have amounted to about £2 per worker, and the initial subsidy to something under £1 10s. per worker, the subsidy being heavily weighted towards the first years of the service. The initial subsidy income ultimately required will depend entirely on the speed of growth of the service, and a safer operating figure would be £2–3 per worker.

11. In terms of a national occupational health service, the Harlow pattern, itself based on the Slough pattern, should be widely though not universally applicable to medium-sized and small industrial establishments. Though ultimately such a service ought to be self-supporting, it would probably require an initial non-recoverable expenditure of £5 million per million workers covered, of which £2 million would be capital expenditure. The ultimate running costs of such a service, carried by industry itself, would probably be £1·5 million per annum per million workers covered.

12. In mid-1956, there were 9·25 million industrial workers engaged in manufacturing industries in factories.[14] If it is assumed that rather less than half these workers are already covered by their own factory medical departments, a non-recurring national expenditure of about £25 million would be needed to launch cooperative industrial medical services for the remainder.

13. The numbers of other workers in civil employment are given in table IV.

TABLE IV—WORKERS IN CIVIL EMPLOYMENT OTHER THAN FACTORIES IN MID-1956 [14]

Group	Occupation	Workers (thousands)
1	Coal and other mining	858
2	Gas, electricity, and water	376
3	Transport and communications	1730
4	Agriculture and fisheries	1032
5	Building and contracting	1541
6	Distribution	2870
7	Professional, financial and miscellaneous	4173
8	Public administration	1300

The great majority of the workers in groups 1 and 2, and many of those in group 3, are already covered by efficient occupational health services. Building and contracting workers could in many places be covered by mobile extensions of cooperative services, at a non-recurring initial national expenditure of £1 per worker. A similar figure might apply to distributive workers, whose physical hazards are comparatively low, but for whom special units in areas with much distributive trade might be needed. Owing to the physical scatter of group 4, it is impossible to estimate either need or cost of occupational health cover.

14. Assuming that running costs are carried by industry, the non-recurring national expenditure needed to provide occupational health cover on a national basis for the majority of those for whom there is now no provision might be of the order of £30 million. Such an estimate is tentative in the extreme.

15. The immediate need is for more experiments in cooperative provision on industrial estates and more particularly in the older industrial areas.

Dr. Garland's project at the Central Middlesex Hospital has already been mentioned. Another such experiment is starting on Tyneside under Prof. R. C. Browne.[15] These

14. Annual Report of the Ministry of Labour and National Service for 1956. Cmd. 242.

15. Second quinquennial report of the Nuffield Department of Industrial Health, King's College, Newcastle (University of Durham); p. 38.

projects have been launched with financial help from the Nuffield Foundation and the Nuffield Provincial Hospitals Trust. Further large-scale experimentation will only be possible if a substantial sum of money is available to enable experimental services to establish themselves.

In the creation and running of the Harlow Industrial Health Service, many people and organisations have cooperated. Without the assistance of the Nuffield Trust, the service could not have been brought to birth, and the successive secretaries of the Trust, Mr. L. Farrer-Brown and Mr. G. McLachlan, have given much wise counsel. Further financial help is being received from the Perry Watlington Memorial Trust.

The industrial employers of Harlow have responded with equal generosity and enthusiasm, and special thanks are due to the first three chairmen of the council, Mr. L. E. Norton, Mr. H. F. Maton, and Mr. F. T. Christmas. The Harlow Trades Council has been a valuable ally, and all the statutory health and local authorities of the area have given practical support; special mention must be made of the North East Metropolitan Regional Hospital Board's help with physiotherapy. Many individual members of the Association of Industrial Medical Officers have assisted in converting us from amateurs into embryo professionals in the sphere of industrial medicine.

The general practitioners of Harlow have responded to the opportunity, and are proving that the part-time industrial medical officer can make a real contribution to such a service. Special thanks are due to our senior visiting medical officer, Dr. W. N. Booth. The consultants of the service have been generous in both time and advice. The major burdens of day-to-day work have been carried by the service's sisters; special thanks are due to Sister P. Braund, I.N.C., our senior sister-in-charge. The other staff of the service have set fine standards of cheerfulness, politeness, and attention to duty.

Finally my personal thanks are due to Miss Joan Payne, the service's secretary-administrator, who has carried the full burden of detailed administrative work; and to Mrs. B. N. Dunce, my secretary at the offices of the Nuffield Provincial Hospitals Trust, who dealt most efficiently with some hundreds of documents and reports.

PRESCRIBING COSTS

Report of Scottish Committee

THE Scottish Committee on Prescribing Costs * were appointed in June, 1957, " to enquire into prescribing practice in the General Medical Service and in the Hospital and Specialist Services in Scotland, with particular reference to the factors governing cost; and to make recommendations ". Written evidence was received from 37 bodies and persons and oral evidence from 28. The committee's report has now appeared and we publish below some points from it.

GENERAL MEDICAL SERVICE

The committee attempted a limited examination of statistical material to see whether there was any correlation between high costs and some possible causes.

They compared the costs of doctors in areas of high and low density of population and doctors with large and small lists, they related claims for sickness benefit with prescribing costs in the four cities, and they obtained figures comparing pre-war and post-war days of sickness absence of the insured population. But they felt unable to draw reliable conclusions from these analyses as to the cause of unduly high costs. Younger doctors had a higher average cost per patient for drugs than older doctors, but " this deduction is of little use by itself ". Surveys and close analyses were not attempted, because it was very doubtful whether " the delay which was bound to be caused would, on balance, have been found to be to advantage ".

* Sir JAMES DOUGLAS, chairman, Prof. STANLEY ALSTEAD, P.R.F.P.S., Dr. A. STEWART HENDERSON, Prof. R. B. HUNTER, F.R.C.P.E., Dr. J. C. KNOX, Dr. E. V. KUENSSBERG, Dr. J. R. LANGMUIR, Mr. D. MCCALL, PH.D., F.P.S., Dr. OWEN MCDONAGH, Dr. E. G. OASTLER, F.R.C.P., Prof. T. B. SMITH, Q.C., Mr. J. C. STEWART, C.A. The secretary of the committee was Mr. F. H. COWLEY.

Conditions of Practice

Instead the committee examined the doctor's conditions of service to find any factors which might be expected to limit the competence of his prescribing, and thus dispose towards wasteful expenditure. Did existing training and conditions of practice permit good practice in the general sense; and secondly, in the circumstances in which they work, were doctors able and could they reasonably be expected to have regard to the relative costs of similar preparations?

The medical student may overlook the fact that hospital patients are not characteristic of the general run of patients in general practice, many of whom could be expected to recover just as safely and quickly without drugs.

Conditions in general practice were often such that the practitioner did not have time enough to get to know his patients properly, and he would be tempted to satisfy the patient with a prescription, thus reinforcing the " medicine habit ". The committee were convinced that " many patients, no less than doctors, now sense that their need is more often for the doctor to find time to get to the root of their trouble, than it is to be given medicine ". With the present form of remuneration, doctors were open to pressure by patients to prescribe drugs or sometimes a particular drug. Though specific and outspoken pressure was not common and most doctors withstood anything so blatant, " the desirable freedom to change doctors which patients enjoy does mean that, whether or not a word is spoken, a patient expecting drugs and who is disappointed can cause a loss of one or several capitation fees. The sensitiveness of doctors to this situation is not lessened by a small minority who have undoubtedly augmented their practices by unashamedly lavish prescribing ".

It was very difficult for a general practitioner so to keep abreast of progress in therapeutics that he could prescribe with maximum efficiency and thus with economy. It was questionable whether the flow of advertising literature could provide a basis for the proper selection of drugs. Sometimes it was comprehensive and authoritative; sometimes it was an oversimplification; and " unfortunately there is a third group where the information is misleading and goes far beyond the mere purveying of information, doing much to undermine a rational and critical approach to prescribing by doctors."

Under these conditions of practice, the committee would not be surprised to find some prescribing that was inefficient and unduly costly. The pressure to which a doctor is subjected makes it difficult for him to attend to tiresome details of relative prices. " Quite high costs may be the cumulative result of innumerable and small acts of omission on the doctor's part, not one of which seems in his eyes—or indeed in any sympathetic observer's eyes—particularly culpable."

Possible Restrictive Measures

The committee believe that, despite the efforts of general practitioners to prescribe as efficiently as they can, there is undoubtedly a considerable amount of wasteful expenditure on drugs in the General Medical Service attributable to imperfect prescribing practice. Discussing " restrictive " measures, and the doctor's freedom to prescribe, the committee point out that before the National Health Service the doctor did not have this wide latitude in prescribing, when he needed to consider the ability of patients outside the National Health Insurance scheme to pay for the drugs he prescribed. The objection to restrictions on prescribing had its crux in a fear of " bureaucratic interference ". In the committee's view, modest restrictions (a limited list of drugs, for example) would be no more serious than the limiting influence of lack of knowledge. But " the probable and understandable unease of the profession in the face

of any such limitation is in our opinion too high a price to pay for the marginal financial savings which . . . seem all that would be likely to be gained ".

Nevertheless the committee considered the following possibilities:

Limited list of drugs.—They did not support the introduction of such a system, but they advocated that doctors should voluntarily adopt the British *National Formulary* as the basis of their prescribing and that the Department of Health should urge its consistent use.

The " black " list.—Such a list might comprise many of the drugs in Cohen categories 5 and 6. There was no guarantee that the saving would justify this circumscription of the doctor's discretion. But the committee recommended that the Department of Health use all possible means short of prohibition to discourage the prescribing of drugs in these categories and that local medical committees ask general practitioners to justify the prescribing of them where their use is disclosed.

Limited list of diseases.—It was considered quite impracticable to draw up a limited list of diseases for the treatment of which medicines might be charged to the Drug bill.

Limitation on quantity of drugs prescribed at any one time.—In New Zealand the Drug bill was much reduced by limiting the quantity of certain drugs prescribable on any one occasion to a 15 days' supply. If it were decided to adopt such a system, it should be given a trial in perhaps one or two executive-council areas to compare the results with the costs of other areas. There would have to be exceptions for chronic sick cases.

Financial ceiling.—After discussing the imposition of a financial " ceiling " on individual doctors by means of an agreed dispensing capitation fee per patient per year, the committee decided that this would not really avoid the main problem inherent in the idea of a ceiling.

Their general conclusions were that such restrictions would not really touch the question of good or economical prescribing. " Having in mind what we have read of experience abroad, we consider that extravagance cannot in practice successfully be confined by prohibitions on prescribing practice. And further we doubt whether the features of many of the restrictive procedures operated abroad could be introduced without detriment to the patient."

Dispensing Doctors

Payments to dispensing doctors for the drugs they supply average considerably less per patient than the drug costs of doctors who write prescriptions for dispensing by chemists. Though the comparison was not a simple one, the committee considered that there was a moral to be drawn—that where doctors were more aware of costs and where they worked from a familiar and not too extensive range of drugs, their costs did appear to be lower.

Prescription Charges

While it was important to try to reduce the pressure on doctor's time, this should not be attempted by increasing prescription charges. At the same time the committee did not suggest that with the charges at their present level there was justification for their removal.

Educative Measures

The committee recommended that teaching hospitals should accept that instruction in economy in prescribing is primarily their responsibility; that hospitals should arrange courses on the cost of prescribing for both senior medical students and junior medical staff; and that medical schools should send all students to work for a period with a general practitioner, and should consider arranging more postgraduate courses for general practitioners.

Prescribers' Notes should be issued more frequently, be made more topical, and include terse and candid notes giving an independent evaluation of new drugs as soon as possible. Thought should be given to combining the lists of preparations in the *National Formulary*, and their costs, and the type of information in *Prescribers' Notes* about new drugs into a comprehensive prescribing handbook.

Prescribing Statistics

The issue of prescribing statistics to general practitioners should be speeded up so that if possible they were in doctors' hands within four months of the prescribing. When a general practitioner's costs were over 50% above the area average for two consecutive issues of the statistics, then, automatically, a panel appointed by the Secretary of State should investigate them and recommend the withholding of remuneration if excessive prescribing was found. Where excessive prescribing was found substantial penalties should be imposed.

HOSPITAL AND SPECIALIST SERVICES

The Department of Health should arrange with regional hospital boards that hospital prescribing committees should be set up throughout the service. These committees should institute costing of hospital prescribing, relating particular consultant posts to defined areas of responsibility for prescribing, and they should consider requiring junior doctors to obtain the counter-signature of the chief of the unit on prescriptions they write for unfamiliar expensive drugs.

The central health authorities should consider augmenting the editorial board of *Prescribers' Notes* so that the publication may provide prompt information on new drugs. The *National Formulary* should be issued to hospital doctors as well as to general practitioners.

Representatives of drug manufacturers frequently obtain access to hospitals without appointment and may thus press their latest drugs on all grades of hospital doctor. The committee would welcome an extension of the practice whereby representatives wishing to call are required first to approach an administrative officer or the chief pharmacist, except where a prior appointment has been made with a chief of unit or senior consultant.

It was from outpatient departments that many of the recommendations to general practitioners to prescribe costly new drugs were made. In Scotland outpatient clinics were often taken by doctors of no great seniority. Where possible outpatient departments should be conducted by more senior consultants, including the chief of a unit and his first assistant.

THE DRUG MANUFACTURING INDUSTRY

The committee hope that some of their recommendations will make doctors more critical of advertisements than they are at present. The request made by the Association of British Pharmaceutical Industry to their members to show the prices of drugs in advertisements was a most useful step in helping the doctor to have some idea of relative costs.

The Association should be invited to cooperate further by asking its members to include in their advertisements the Cohen classification where one had been given, and, where the drug had not been classified, to indicate the fact. The price, the Cohen classification, and also the approved name should be shown together within a small " box " of standard shape and size on all printed advertising matter circulated to doctors in the National Health Service.

Much of the industry's sales promotion was carried out by representatives who visited both general practitioners and hospital doctors. Some of these representatives were well-qualified persons whose visits were informative and appreciated, but many representatives were skilled primarily in the art of persuasion.

The committee deplored the practice of some manufacturers or their agents in quoting what was sometimes only superficial discussion between a representative and

a consultant as an endorsement for a preparation on which no thorough trial had in fact been carried out. Medical practitioners should be on their guard both against giving their approval to preparations the efficacy of which they had not full examined and also against manufacturers' claims when it was clear that no evidence of a proper trial existed.

Bad prescribing practice summed up in the words "blunderbuss" therapy had a bearing on the policy of drug manufacturers. When a manufacturer offered preparations of the blunderbuss type he often referred in his literature to clinical concepts entirely unacceptable to critical clinicians. Moreover it was suggested sometimes that the preparation was compounded so comprehensively and "blended" so ingeniously that it had merits quite beyond the reach of conventional methods of treatment. This approach, the committee was satisfied, must be dismissed as an ancient form of quackery assuming the guise of modern pseudo-science. If doctors could be persuaded by manufacturers to use such preparations it was clearly no easy matter to restrict "blunderbuss" therapy, but the appropriate bodies should, nevertheless, consider ways of preventing or reducing it.

The committee discussed the question of whether a central body should be set up whose approval would be necessary before any new preparation could be marketed. Before this approval would be given, evidence would have to be submitted to show that the drug would be useful and safe, and that it offered significant advantages over existing preparations. The difficulty was in deciding whether such a regulative scheme would result in a worthwhile saving in costs. It was very questionable whether, even if the variety of drugs were reduced, the costs of the remaining brands would fall. "Unless an appreciable economy were assured, we would not feel justified in recommending the institution of an elaborate restrictive scheme for the marketing of drugs in the United Kingdom."

EXTENSION OF THE ROYAL MARSDEN HOSPITAL

New Hospital at Sutton

IN 1949 the Ministry of Health suggested that the proposed new radiotherapy unit for the Royal Marsden Hospital, in London, should be developed on the site of the Downs Residential Nursery at Sutton, Surrey. Detailed plans were approved in December, 1950, and since building started at the end of 1953 three units have been housed there. A hostel of 12 beds accommodates patients being treated with cæsium 137 (Sutton is the first teletherapy unit in this country to use this source of radiation) and is associated with an outpatient consulting-room; another building has been converted to house a radiophysiological section of the physics department, and a third is at present shared by the Radiological Protection Service and the South Metropolitan Cancer Registry.

Further building on this 30-acre site is planned in three stages.

In an *interim stage*, to be started soon, the remaining buildings will be converted for use by the radiological protection service, which investigates the harmful effects of X rays and radioisotopes, and the physics laboratories. Because of its low natural radioactivity, chalk from the local subsoil is to be used to screen a second low-background laboratory; in this it should be possible to measure extremely low levels of radiation.

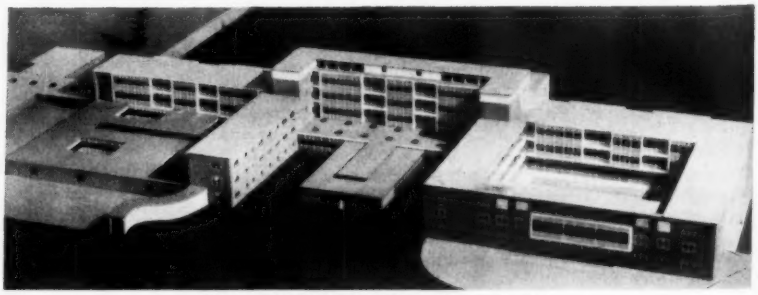
The *first stage* of the main development is estimated to cost £800,000, of which £600,000 is to be allocated by the Ministry of Health, and £200,000 by the board of governors of the Royal Marsden Hospital. A further £250,000 is needed to install a 35-million-volt linear accelerator; with this the relative advantages of supervoltage and conventional radiotherapy could be compared. At present it is hoped to fit at least one 4-million-volt linear accelerator in the radiotherapy department, possibly two, since there are great advantages in using a pair of these machines together. Building should start this summer, and at the end of the first stage the hospital will consist of two 25-bedded wards; one 40-bedded ward for ambulant patients, who require little nursing; an outpatient department; pathology and diagnostic radiology units; and administrative and other offices.

The *second stage* will complete the hospital and add 75 more beds; a permanent operating-theatre and a radioactive-isotope unit will also be built.

Since 1944 some sixteen hospitals, in both London and the southern Metropolitan area have been associated with the Royal Marsden Hospital in the treatment of neoplastic disease. This new centre for radiotherapy, particularly in the supervoltage range, will provide treatment for a whole group of teaching and regional-board hospitals. Furthermore, it is hoped to provide visiting doctors with laboratory space, and to arrange regular short-term courses on the use of isotopes for post-graduates.

As the site at Sutton runs from east to west, all three ward blocks are to be placed facing due south, giving all the ward bedrooms a sunny aspect. A high degree of standardisation of the various building components is to be achieved by planning to a module of 3 ft. 4 in.; thus the size of most of the rooms will be multiples of this, and variation in size of built-in furniture and fitments can be reduced. Externally the building will be faced in brick and specially textured concrete panels. Where large windows are required for light and air—e.g., in the wards—the whole of the external wall will be clad in coloured panels.

The architects for the Royal Marsden Hospital were Messrs. Lanchester and Lodge.



The completed hospital from the south-east.

The Widdicombe File

LIII. OVERLORD

DEAR JOE,

I got quite a surprise the other day when I read the weekly calendar for a surgical firm and came to Tuesday "Mr. Pinkfoot. Operations. All students in theatre"; it was the same for Friday. Didn't you think this was a thing of the past? How well I remember the Thursday afternoons in my own studenthood—from 1.30 to 7 P.M. or later watching the master doing the same operation as often as six or seven times. How I longed to see really catastrophic bleeding to relieve the tedium! But he was too good; though occasionally he enlivened the proceedings by a display of animosity towards his house-surgeon or his assistant. However, we did have the tea-break to look forward to (that saved me a valuable sixpence in my daily budget); and we were permitted to act as porters.

I was surprised also because Pinkfoot isn't one who is afflicted with the overlord complex. This, of course, comes out in many ways, and you no doubt know what I mean. I refer to the attitude which in its most blatant form permits a man to rap his senior registrar, a man over 40, on the knuckles; who turns up on Sundays to do a round and expects everyone else to be there too; who is so oblivious of the needs, nay rights, of his registrar that he will burden him with phone calls about trivialities—sending him scurrying hither and thither when he's trying to find a little spare time from the clinical and operating chores to go over to the library or even into a laboratory. We all do these thoughtless things: it's a hazard of a system which gives us so much power over others. I even feel guilty when I leave the abdomen to be closed by the assistant, though he's probably only too thankful to get the old fool out of the way and to do something himself.

It's so much a part of the pattern in surgical life that we often don't notice it. What's worse, we don't recognise the harm it does: that it tends to induce a menial mind in our juniors, who are, after all, grown up (how often I've heard seniors in their late middle age talking of the "young men" when referring to those less fortunate in their appointment but who've nevertheless reached the forties!). And a menial mind is a fettered mind—but that's just what overlord wants, for life's easier that way and it flatters his ego. Though he forgets that thus he renders himself uncivilised; that his failure to regard his junior as a man of full stature with full rights may end in failure to respect the rights of his patients. I'm sure we can both think of examples of the doctor who behaves as overlord to his patients ("No good explaining things to 'em", he says; "they wouldn't understand") and the surgeon who either tells his patient nothing or simply that he's to have an operation.

But don't think that overlord is a surgical sin; it just happens to be more manifest in the surgical system. It's all-pervading, often insidious, always stultifying. I know hospitals where registrars are forced to be resident, even though not on duty, in order to comply with some petty regulation, and are thus quite unnecessarily denied home life in their early married years and given the added financial burden of running a home and paying the hospital to boot. This is inhumanity and wouldn't be tolerated outside our profession—probably not outside teaching hospitals (we can't call them university hospitals while such behaviour continues). Equally inhuman is the overlord who insists that his juniors should write the case summaries longhand before passing them to the secretaries for typing—on the excuse that dictation wastes secretarial time (a dictaphone is also inadmissible on the score of expense). It would matter less if they *were* summaries; but they grow into extensions and take anything up to two hours each evening to complete—time which could usefully be put to reading, research, or even simply to leisure. But overlord doesn't recognise leisure: "I had none when I was your age, my boy"; or from the more academic type: "Medicine is a whole-time occupation from which there can be no spare time." And overlord takes no overt leisure himself but finds it in laudable peripatetic ways—for which his juniors are ineligible.

There's the committee form; and though you may think, not without reason, that the deliberations of committees are so fruitless that they could hardly be stultified, there are occasions when it does real harm—usually on university committees. You haven't yet been in a position to watch a medical faculty at work. There, those of sub-professorial status are submitted to the treatment. They are in the minority; they are to be seen (to give an appearance of democracy) but if possible not heard; their opinion is not sought and any attempt by one of them to speak is discouraged by looks of disdain from the chair and lack of interest from the professors.

But there's a more interesting method by which some exercise overlordship, interesting because it represents a form of social atavism. You've doubtless seen the colony of baboons on Monkey Hill; they have an interesting hierarchical system whereby one male, more aggressive than the rest, works his way to the top by combat and is then recognised as king. In this position he spends most of his time aloof, not deigning to take part in the affairs of the lesser fry arguing on the rocks below. Nevertheless, it's obvious that while he affects unconcern he has half an ear cocked. Any challenge to his view, and he ups and waves those strange ugly cushions on which he sits; this display of anger frightens, even sometimes to death, and suffices until he gets too old—when a strong young upstart will have the courage to challenge in his turn and supplant him in battle.

In our faculty we have a king and a prince; one takes over when the other is visiting distant hills. Though modesty, otherwise unnatural to them, demands that neither simulate the baboon exactly, each displays to a nicety assumed anger at any sign of a contrary opinion from the non-professorial lesser fry, and so frightens the assembled company as to make further discussion appear both improper and impertinent. It's a delight to watch.

Overlord is perhaps most insidious in the disciple-maker, the didactic teacher, the man who'll brook no alternatives, no contrary view. I've seen disciples who've gone through life with the catch-phrases and even the grimaces of the chief. It's insidious because it's sometimes disguised by a veneer of paternalism. In fact, in a teaching centre, paternalism, however genuine, is dangerous; for it lies at the top of the slippery path to overlord. So beware of the man who speaks of the students as "the boys" or "the lads"; he's about to possess their minds instead of freeing them—if he hasn't done so already.

Yours ever
P. G.

In England Now

A Running Commentary by Peripatetic Correspondents

MEDICINE is wonderfully cinematogenic, and it vies with Law as the most telegenic of professions. Alas, it is also exceedingly unpictorial. The sheer number and variety of pictures which make up the 191st exhibition of the Royal Academy is exhilarating—the exhilaration being only slightly damped on closer acquaintance—but only a few of the exhibits are in any way medical. There is *The Waiting Room* by A. R. Thomson, R.A.—humorously anecdotal without being too literary. The patients seem real, surrounded by an atmosphere of anticipated doom, anxiety, and resignation; only the doctor has that clean cheerful profile which one associated with advertisements for antacids. *The Visitor* by Stella Marsden is excellent fun: it almost persuades one that painting is the right medium for capturing the embarrassment, the inanity, and the mutual agony of visiting-time in the ward. (But what is Matron doing in the ward at that hour? And unattended, too!) On the whole, however, one must sadly conclude that our nurses are still without their Dégas: they are even without their Sir Alfred Munnings. And yet . . . and yet . . .

As sitters for portraits, doctors do not usually excel. A good portrait is a joint effort: if the painter must get outside himself sufficiently to understand his sitter's mind, the sitter too must allow his face to become more than a mask. Doctors may not carry their bedside face to bed with them; but they tend to slap it on firmly at the faintest whiff of oil and turpentine. A portrait of Sir Samuel Gurney-Dixon, as pro-chancellor of the University of Southampton (by H. Andrew Freeth, A.R.A.), is a competent academic affair; but it is perhaps just as well that medical faces are fewer this year than for some time past. One's only fear is lest our ancient medical institutions have given up all pretence at being patrons of visual art in favour of the televisual. This would be a pity; one of the world's best portraits is medical; and it still hangs, if not at Burlington House, only a stone's throw from it. And at the National Gallery Goya and his sitter (Dr. Peral) even manage to provide one of the most fascinating clinical short cases of ? facial palsy.

Past the pictures and sculptures, a small room is reserved for the year's architecture. It contains some splendid models and drawings of blocks of flats, schools, libraries, factories, and office buildings. There is an exciting new clubhouse designed for the International Club at Gibraltar and a fabulous-looking palace for Kuwait. No hospitals.

* * *

The other day at the end of the first half of a long operating-list I asked the theatre sister to arrange to have some sandwiches sent across to save me the time of changing and going to the lunch room. She was referred to the hospital catering officer who said to her, "If he can't come to the cafeteria to collect them, let him bring his sandwiches in with him like everybody else. It's time these surgeons were deglamourised."

* * *

Another application of the Law of Inverse Squares relates to the efficiency of a hospital to the total number of medical and clerical staff employed. Thus at one extreme I can imagine some palatial chromium-plated institution in which the house-governor, deputy house-governor, assistant house-governor, et al., all have suites of rooms (of declining opulence) and a covey of secretaries (of decreasing glamour), and where gallery after gallery of record offices are filled with the efficient sound of typewriters and quiet bustle of uniformed clerical staff carrying notes here and there, and there and here. Yet where the patient, as he queues for the third hour (waiting for someone to locate his card, or the doctor, or the nurse, or the other doctor, when they find he isn't Mr. E. Smith, patient of Dr. Higgins, but Mr. E. E. Smith, patient of Dr. Dickens), fails to appreciate the smooth efficiency. So does the outside doctor making a routine inquiry about one of his old patients. He assiduously copies out the reference number: P/MNQ/OZ.1954/P.1190/iii/Dr. Green, and after seven weeks gets a short reply about a totally different patient; or the seventh copy of a misspelt summary, washed illegibly in the sands of time; or a regret that they cannot trace the patient ever having attended; or nothing.

Take the other extreme—the hospital where they stack case-notes as they come, on shelves. They may have a system of reference numbers, but the mere name of the patient seems enough to obtain the case-records in their entirety by return of post, registered. These hospitals employ a couple of part-time secretaries to every 1000 beds or so. The administrator is usually medical, but perhaps this is a coincidence. As a rough general rule one may always take it that the length of reference number to the patient varies inversely with the efficiency of the organisation that has found this number necessary.

* * *

A tall wooden fence surrounds the building site and effectively prevents the casual passer-by from stopping to watch other people at work. But the Medical School overlooks the site and is a perfect grandstand. We can sit in our rooms and laboratories and watch in comfort the progress of the building below us.

First came bulldozers, mechanical diggers, and automatically tipping lorries, effortlessly tearing up the ground and removing vast mounds of soil and rubble. Now mobile cranes, cement-mixers, and self-propelled trucks have taken their place and are erecting steel girders and covering the hole in the ground with a sea of cement.

Only a handful of workmen are to be seen on the site, doing little physical work, but controlling and directing the pieces of machinery. One man is constantly hard at it. He is slave to an automatic shovel, unceasingly feeding the correct proportions of sand and cement to an enormous, yellow, cement-mixer.

All this automation is presumably designed to save time, money, and effort. Sometimes I wonder just how much time, money, and effort is being wasted by the unproductive gazing-out-of-windows of half a dozen professors, several lecturers, and whole classes of students?

* * *

It was a long conference. Over twenty papers were read and almost every lecturer began something like this:

> "We investigated the effect of bovine-leontinic-49-keturic acid on the placid gland of the polar skunks. First slide please. Now, this slide shows that bovine-leontinic-49-keturic acid has really a structure which is *not* identical with that originally described by Lagauche and Lavache. We used, however, their original preparation, which for short we shall call BK49K2, and we can see its effect on female baby skunks weighing 250 g. on the next slide."

And so it went on, slide after slide; once I counted 30 slides in 25 minutes (15 minutes was the official time allowed for the paper). After BK49K2 was exhausted, the effect of AS54498 was discussed. The lecturer completely ignored the red light, indicating that 20 minutes had been exceeded, in the flush of racing home more and more slides of densely packed, far too small, illegible figures, dots, and curves. The climax was a barley visible chromatogram of bunkum in the earfluid of bats.

* * *

In the Garden—VII

CALL ME *Schizophragma mlokosewitsch* AND LET THE WORLD GO BY

I sometimes wonder, like the Persian bard,
Why botanists must make the names so hard.
And why the first to find a lovely flower
Must with his name for ever leave it marred.

How simple if instead of standing dumbly
In front of Teuto-Russian names uncomely,
We gave them easy English household words
Like Marjoribanks, Fiennes, the Beauvoirbrook, or Cholmondeley.

Letters to the Editor

THE CRANBROOK REPORT

SIR,—One of the most interesting aspects of the recently published Cranbrook Committee's report is the paucity of letters about it in the medical press. Some say this reflects despair at the committee's failure to unify the maternity services: for myself I believe it reflects two things—the extreme complexity of the problem of providing a good maternity service, and the widespread lack of knowledge as to what really is right and what is wrong in the present set-up.

I used to be very critical of the tripartite division of the service (hospital staff, local authority with the domiciliary midwives, and general practitioners), but now I am not so sure. Looking back to the days before the National Health Service, these three groups largely went their own way with very little overlap of responsibility, and consequently very little treading on toes. Now, each group is becoming more and more involved in the others' affairs, and here and there there has been friction. The trouble is not so much the division of responsibility as the fact that we have not always worked together as a team should: indeed some have not yet come round even to thinking of teamwork as being the order of the day for the new obstetrics. The worst faults include lack of liaison between interested parties and the monopolising of the patients. For example, how can we recruit domiciliary midwives, and expect them to be content in their work, if they are debarred from antenatal care, by general practitioners who do not take the trouble to see that the midwives working with them have a chance of professional fulfilment. If the specialist goes it alone some of the family doctors will be disgruntled. The midwife, too, is not blameless; for she may be too possessive of the patient, or resentful of a medical point of view she does not really understand.

Frankly, I doubt if we are ready yet for a unified service, for I don't think it can be put in the charge of any one group until that group as a whole has shown itself sufficiently enlightened to command the respect and trust of all, and such is not the case now. Maybe in time, when the local liaison committees as recommended by the Cranbrook Committee have been set up and have got into their stride, and when there is more respect for the contribution the other fellow can make, a unified service acceptable to everyone can be contrived. At the moment, it may even be safer for the patient that the service is divided—at least this discourages monopoly and gives the patient some choice.

Let us therefore welcome the divided (I prefer the word "shared") responsibility, and get on with the task of strengthening the team at local professional level. One final point, let the composition of the local professional liaison committees be such that no one group is in a position to lord it over the others.

Department of Obstetrics and Gynæcology,
Jessop Hospital for Women,
Sheffield. C. SCOTT RUSSELL.

COLLEGE OF PATHOLOGISTS

SIR,—Your correspondent XYZ, in his letter last week, has omitted certain relevant considerations from his plea that pathologists should be members of the Royal College of Physicians. The pathologist does not serve only the physician, but also the surgeon and the gynæcologist, and the training leading to the higher diplomata of the other two Royal Colleges is, a priori, as valuable to him. In addition, it is becoming increasingly necessary for him to possess a wide knowledge of non-medical science, particularly of biochemistry and of physics.

Assuming that there must be some limitation to his post-graduate studies, it seems more appropriate that the would-be pathologist confine himself to a training that will equip him to practise all branches of pathology, than that he should seek to become an abortive physician, surgeon, and/or gynæcologist. It must be conceded that the Royal Colleges are not likely to confer their much-prized qualifications on those trained largely in the laboratory, but rather on those whose experience is mainly clinical; similarly the pathologist must be well trained in his multifarious duties, covering a wide field of chemical and biological experience. It is no longer sufficient that a medical graduate should pick up a handful of rule-of-thumb techniques. The physician turned pathologist is a product of the honourable past.

Necessarily a pathologist must understand the point of view, and speak the language, of the clinician, and he must not be divorced from the life of the wards and of the clinic. Surely it is to this end that he must undergo the discipline of his undergraduate medical training and of his postgraduate hospital experience. Thereafter let him study pathology, the wide ramifications of which will tax his intellect to the full. And let the depth of his learning be suitably tested by a rigorous, and appropriate, examination which shall include not only the theory and laboratory practice of his work but also its application to every branch of clinical practice.

The laudable anonymity of your correspondent leaves it a matter for speculation, but one cannot help wondering whether he may work in a restricted field, perhaps in a special hospital, and whether he is aware of the range of knowledge of medicine, in the broad sense, and of general science that is required of the general pathologist today. Or does he envisage yet narrower specialisation into physician pathologists, surgeon pathologists, obstetrician pathologists, public-health pathologists (D.P.H. Path.!) and general-practitioner pathologists?

City Hospital, Nottingham. J. B. FOOTE.

SIR,—The idea of establishing a College of Pathologists with the prime object of issuing yet another higher qualification seems to me to be fundamentally unsound. In fact this was only one of six aims and objects set out in the memorandum on the proposed college by the Association of Clinical Pathologists, but the other five seem to have faded into the background in the subsequent discussion. There are far too many higher diplomas already, and if a specific one in pathology was so desirable the D.C.P. and diploma in pathology would have proved more popular. This country has become diploma-crazy, with little real evidence that success in factual examinations is of any true value in assessment of ability. The great pathologists of the past often had no higher qualification at all and no-one thought the less of them.

A College of Pathologists would do great service, and command respect and support from the profession as a whole, if it forgot about examinations and concentrated on improving laboratory accommodation, research, and training facilities. What is needed now is a conversion of the pathology laboratory from the Cinderella of the hospital into what Prof. A. V. Neale has termed "that Mecca for the constructive clinical chat".

Department of Pathology,
The Radcliffe Infirmary, Oxford. MICHAEL S. DUNNILL.

POLYCYTHÆMIA

SIR,—Your leader of April 18 calls for comment on a number of points. These we make in the light of our own experience at this centre where well over 100 patients with polycythæmia vera (mostly under the care of Dr. J. B. Harman) have been treated with radioactive phosphorus during the past ten years.

Detectable splenomegaly is by no means a constant finding, being present in only just over half of our patients. Nor have we found it difficult to distinguish between the primary and secondary forms of the disease.

^{32}P, combined with venesection where indicated, is at present established as the treatment of choice for the majority of cases.[1–5] In our group of patients the average remission between treatments is twenty months. Unless admission is indicated for investigation and other treatment, all our patients are given ^{32}P as outpatients (usually not more than 5 mC).

On the vexed question of the possible induction of leukæmia by ^{32}P therapy, it is the opinion of J. H. Lawrence, who has by far the largest series in the world treated by ^{32}P over the past twenty years, that there has been no increase in the incidence of leukæmia over that reported in groups treated by conventionl methods, while the number of deaths from vascular complications had been reduced by one half since the advent of ^{32}P. In spite of the theoretical danger of the genetic effect of ^{32}P, no harmful effect has been seen in practice. Furthermore, healthy children have been born to patients who have been treated in this way. In our opinion, the possibly lifesaving effects of treatment with ^{32}P should not be denied to younger patients, and certainly not to those with an expectation of life as low as seven years.

Remissions induced by the HN_2 group of drugs appear to be short, and the treatment is accompanied by unpleasant side-effects (which are never seen with ^{32}P), and is not without risk of excessive bone-marrow depression and local venous thrombosis. One or two small series of patients treated by busulphan have been reported,[6 7] and this drug would seem to be of use though it is too early yet to comment on the length of the induced remissions. Occasional cases appear to be resistant to treatment even with large doses of ^{32}P. 3 of our patients (less than 3%) who fall into this category have been treated with busulphan with encouraging initial response.

Royal Marsden Hospital,
London, S.W.3.

O. GARAI
E. M. LEDLIE.

SIR,—Your leading article of April 18 says that " no-one any longer administers phenylhydrazine or its derivatives ".

With proper shame I confess that of the ten patients with polycythæmia vera whom I have seen in recent years I have treated three with phenylhydrazine hydrochloride, over periods of 13, 12, and 5 years, their ages at the start of treatment being 40, 29, and 69 respectively. Their blood has been continuously and satisfactorily controlled throughout this time, although in the first few months there was some difficulty in finding the maintenance dose of the drug. They now visit me about once a year, and that is usually needless. Their early supervision required personal attention and was not delegated to juniors. There is no " routine ". Some patience is needed but no needles. The disadvantages of ^{32}P so ably summarised in your article are avoided, and also the unpleasantness of mustine and bleedings.

As an assiduous reader, I seem to note an increasing dogmatism in the pronouncements of experts. Does this come perhaps of thinking in terms of disease and not of the personal quirks, situations, and feelings of patients? Perhaps it is because such things are left to juniors as being of little importance beside the disease.

Plymouth. C. R. CROFT.

1. Lawrence, J. H. Polycythæmia. New York, 1955.
2. Stroebel, C. F. *Proc. Mayo Clin.* 1954, **29**, 1.
3. Fountain, J. R. *Brit. med. J.* 1957, i, 1335.
4. Harman, J. B., Hart, P. L. de V., Ledlie, E. M. *ibid.* 1955, i, 930.
5. *ibid.* 1956, i, 1354.
6. Wald, N., Hoshino, T., Sears, M. E. *Blood*, 1958, **13**, 757.
7. Louis, J. *J. Amer. med. Ass.* 1958, **168**, 1880.

FULMINATING ECLAMPSIA TREATED BY HYPOTHERMIA

SIR,—Wing-Commander Malcolm and his colleagues (April 25) are to be congratulated on their eclamptic patient's response to treatment which included hypothermia; but is it certain that the hypothermia contributed to their success? They admit freely that the convulsions, which had proved refractory to a " lytic cocktail " and thiopentone, ended with the induction of general anæsthesia for the purpose of tracheotomy. Since an isoelectric E.E.G. can be attained by refrigerating the body,[1] hypothermia may well be a rational, lifesaving (if heroic) method of controlling status epilepticus, whatever its ætiology. But I would prefer to try the effect, first, of intramuscular paraldehyde combined with adequate oxygenation, and then of prolonged general anæsthesia, before resorting to body-cooling.

I wonder whether Wing-Commander Malcolm and his colleagues did not place undue reliance on the doubtful anticonvulsant properties of pethidine, chlorpromazine, promethazine, and short-acting thiopentone, and whether it was the general anæsthesia rather than the hypothermia which controlled the epileptic state in this case.

Alder Hey Children's Hospital,
Liverpool. JOSEPH NEVILLE.

MEDICAL CARE OF THE ADOLESCENT

SIR,—The report of the British Pædiatric Association, published in your issue of April 18, is an important document, and it is not for me to comment on many of the suggestions made: but in its references to the School Health Service I feel that on one aspect at least I am entitled to speak. I refer to the sentence: " We believe that the pædiatrician should be increasingly employed in the ascertainment and care of handicapped children."

Now, Sir, we of the School Health Service have cause to be grateful to many pædiatricians for the help so willingly given in assisting us to make a diagnosis, particularly when the defect has been mainly physical. We must also pay tribute to the educationalists and psychologists who have helped us in studying the other aspects of the child.

Those of us who are specially concerned with the ascertainment of handicap feel that the experienced school medical officer is well able to carry out this function, and that not least amongst his duties is the consideration of all specialist reports, to coordinate them, and to make a final judgment. As to the care of the handicapped children this is at present carried out by teams of experienced school doctors, teachers, nurses, and auxiliaries, with consultant opinion as required. I doubt whether this arrangement can be bettered.

May I take this opportunity of indicating a field where I think valuable help could be given us by pædiatricians—in arranging for the hospital admission, investigation, and possible treatment of young children who appear to have a mental defect? I have in mind such conditions as phenylketonuria, hypoglycæmia, galactosuria, tuberous sclerosis, &c., in preschool children, and certain types of brain damage in older children. Such cases are among those who may be brought to the school medical officer, for exclusion from school attendance, present or future, as " ineducable ". On inquiry it is not unusual for the parent to tell us that the child has been seen in some hospital outpatient department a year or so ago perhaps, but dismissed as hopeless, told not to attend again, and no investigation suggested.

1. Drew, C. E., Keen, G., Benazon, D. B. *Lancet*, April 11, 1959, p. 745.

May I in all humility, Sir, venture to suggest that the pædiatrician should be "increasingly employed" not in the "ascertainment and care" of handicapped children but in the detailed investigation and possible treatment of their handicaps.

P. R. KEMP
Assistant Principal School Medical Officer, Birmingham.

TORULOSIS

SIR,—Torulosis is not a common disease in any part of the world, and its very rarity is a diagnostic challenge because the prognosis is so bad in the absence of early treatment. Too often, at present, the diagnosis is not made until postmortem, or is made during life considerably later than it should be.[1] The presence of torulosis still tends to be overlooked even in cases of those diseases which are known to be specially liable to be complicated by this infection—Hodgkin's disease, sarcoidosis, and other diseases of the lymphoreticular system.[2] Until recently there was no effective treatment for torulosis, unless the disease chanced to be eradicable by surgery, as in occasional cases of pulmonary torulosis and even of cerebral infection—otherwise it was mortal in all but exceptionally rare cases. The introduction of amphotericin B has improved the prognosis greatly, as the preliminary figures of Rubin and Furcolow [3] have shown. Even this drug is no unfailing cure for the disease, particularly for advanced cases, nor is it without dangers, which become greater the longer its administration has to be continued. The need to start treatment early is therefore doubly imperative, and any reminder to us to be on the look-out for the infection is opportune and welcome. It is unfortunate, however, that your recent annotation on torulosis of the nervous system (March 21) should contain much that is misleading, and omit much that is important enough to the clinician to need mention, even within the limited space of an annotation, if torulosis is to be correctly diagnosed earlier and oftener.

It is dangerously inaccurate to state that "*Cryptococcus neoformans* . . . is found in the mouths of healthy people, only rarely causing disease". We know of no sound evidence that pathogenic cryptococci have ever been obtained from healthy people: this must surely be a most unusual event, and not the commonplace experience which you make it sound. Further, while the occurrence of non-pathogenic cryptococci, such as those designated by the late Dr. Rhoda Benham [4] as *C. neoformans* var. *innocuus*, is well known, there are other difficulties arising from the fact that strains of cryptococci from cases of torulosis are often found to show only limited pathogenicity when first isolated, although their pathogenicity is readily enhanced by animal passage, and is liable to fall off again when they are grown on artificial culture media. It is important to appreciate that there is no simple method, other than animal inoculation, of differentiating between the non-pathogenic and the pathogenic strains. It follows that until more is known about the mode of transmission of the organisms all cases of torulosis should be regarded as infectious, and no-one should lightly contemplate the transference of the cryptococcus from a patient with torulosis to the respiratory tract, or even the skin, of another person.

Whenever *C. neoformans* is found in any specimen, from any person, the only safe, practical rule is to consider that this indicates the presence of torulosis, until such time as exhaustive clinical and laboratory studies, and long-term careful follow-up, together show this interpretation to be mistaken. The following case, like others known to us, shows that this is no needless precaution.

A fit young man broke his leg at football. An orthopædic operation was necessary, and following it collapse developed at the base of the left lung. *C. neoformans* was found among the otherwise commonplace flora of a specimen of sputum. The pulmonary collapse cleared up promptly on bronchoscopic removal of a mucus plug, cultivation of which did not yield cryptococci. No other abnormalities were found. As a precaution his chest was X-rayed monthly for five months, and again three months later: on the last occasion a small round shadow was found in the outer part of the middle lobe of the right lung. He had no sputum, and attempts to demonstrate cryptococci in bronchoscopic and gastric washings failed. Lobectomy was done: the lesion was a cryptococcal granuloma. He has had no further trouble.

In such a case the potential importance of finding *C. neoformans* in the sputum would have been overlooked had the patient's doctors shared your erroneous view that this is not unusual.

Your remarks on the incidence of torulosis in this country also seem to give an impression which is scarcely accurate. Although in fact only some 25 British cases have been reported (7 of them in your pages [5–8]), even this number is larger than the reader of your annotation might appreciate, and there is no doubt that there is now a considerable number of unpublished cases of torulosis diagnosed in Britain.

We should like, if we may, to enlarge upon one point in particular in your comments on laboratory methods. It is quite true, of course, that cryptococci may be mistaken for lymphocytes in cerebrospinal fluid unless the centrifuge deposit is mixed with nigrosin or India ink to show the characteristic capsule as a broad clear zone between the cell body of the yeast and the dark background. When the yeasts are numerous in ordinary preparations it is not with lymphocytes that they are likely to be confused but with red blood-cells: this is much likelier to mislead the observer, for large numbers of red cells might be present because of accidental contamination of the sample, whereas the presence of large numbers of lymphocytes would at least indicate that the fluid was pathological. The late Dr. A. L. P. Peeney, of Birmingham, told one of us that he had once had 2 cases of cryptococcal meningitis in quick succession in which the large numbers of cryptococci present in the cerebrospinal fluid were mistaken by experienced microscopists for erythrocytes, and that he had learnt then that the pathologist must always be at pains to satisfy himself that what look like red cells in cerebrospinal fluid are in reality what they seem.

Finally, you did not mention what we believe to be the aspect of torulosis which is of most practical diagnostic importance today—its occurrence as a complication of diseases of the lymphoreticular system. Although this complication is rare in relation to the overall incidence of Hodgkin's disease and other malignant diseases of the lymphoreticular system, and of sarcoidosis, these conditions account for something like a third of all cases of torulosis.[9] The reasons for this association are not clearly known, and are not relevant to our immediate purpose, which is to draw attention again, as we have tried to do before,[2 10] to its occurrence. The possibility of torulosis has always to be considered whenever any patient with any disease of the lymphoreticular system develops any sign of neurological disease (particularly meningitis), or of the onset of pulmonary disease (or alteration in existing pulmonary lesions), or of osteitis, or of ulceration of the skin or mucous membranes. It is true that in most of these cases the condition which draws attention to the possibility of torulosis may prove to be merely a fresh manifestation of the original disease: but something of value will have been achieved if awareness of the alternative leads even occasionally to prompt diagnosis of torulosis and so to the opportunity to begin treatment

1. Littman, M. L., Zimmerman, L. E. Cryptococcosis: Torulosis or European Blastomycosis. New York and London, 1956.
2. Symmers, W. St. C. *Brit. med. J.* 1957, i, 459.
3. Rubin, A., Furcolow, M. L. *Neurology*, 1958, **8**, 590.
4. Benham, R. W. *Bact. Rev.* 1956, **20**, 189.
5. Greenfield, J. G., Martin, J. P., Moore, M. T. *Lancet*, 1938, ii, 1154.
6. Daniel, P. M., Schiller, F., Vollum, R. L. *ibid.* 1949, i, 53.
7. Symmers, W. St. C. *ibid.* 1953, ii, 1068.
8. Beck, A., Hutchings, M. W., Makey, A. R., Tuck, I. M. *ibid.* 1955, i, 535.
9. Zimmerman, L. E. *Amer. J. clin. Path.* 1955, **25**, 46.
10. Plummer, N. S., Symmers, W. St. C., Winner, H. I. *Brit. med. J.* 1957, ii, 599.

with a reasonable hope of overcoming the infection without residual disability. To cure an infection which hitherto has been a killing complication of Hodgkin's disease is worth while: to do the same in the case of a patient with sarcoidosis, which but for the complicating infection might run a benign course, is infinitely more so.

The doctor must be alive not only to the existence of torulosis but also to its ætiology, to the grave significance of finding the organism which causes it, and to the need for early treatment.

Charing Cross Hospital,
London, W.C.2.

WILLIAM ST. C. SYMMERS
H. I. WINNER.

HAZARDS OF WATER ENEMAS

SIR,—The practice of giving 20–30-pint washouts until the large bowel is absolutely free of fæcal matter and gas before embarking on a barium enema is I think rather unnecessary and time-consuming. In this department during the past three months, about half the patients having barium enemas have been prepared solely with bisacodyl ('Dulcolax'). The results suggest that this preparation is an effective substitute for the conventional enema. It is more comfortable for the patient, as well as being a big time-saver for the nursing staff.

Radiodiagnostic Department,
The London Hospital,
London, E.1.

J. G. SOWERBUTTS.

PRISON MEDICAL OFFICERS

SIR,—I feel that it is time that psychiatrists were called on to show some evidence of the existence of their special ability to deal with the problems of delinquency to which they lay such confident claim.

Among the prison population are some psychotic and neurotic patients; likewise there are a number who suffer from conditions which fall within the province of other specialists. For example, the incidence of varicose veins and hæmorrhoids is remarkably high among long-term prisoners. There is nothing to suggest that the incidence of psychiatric diseases is higher among criminals than among the general population. Even where evidence of psychiatric disease is found, it by no means follows that the psychiatric condition is the cause of the misconduct.

I believe that, except in a few rather rare categories, such as some of the sex offences, the proportion of psychoneurotic patients is rather lower among delinquents than among the general population. The neurotic solves his problems by breaking down into neurosis, not into crime.

Criminology is not a branch of psychiatry. It lies in the debatable ground between a number of intellectual disciplines —theology, philosophy, medicine, politics, and genetics, to name only a few. Psychiatry is only a minor, and probably not the most fruitful, contributor to this subject.

I fear that the claims of prison doctors to be considered as specialists are very modest when compared with those of the psychiatrists. Their most important public duty is to help the courts to decide on the question of criminal responsibility, to point out factors tending to mitigate culpability, and to indicate, if asked, which offenders are likely to derive benefit from psychotherapy.

At first glance it seems that this last question can best be answered by a psychiatrist. It is, however, so rare to meet a psychiatrist who will admit that anyone at all, let alone a delinquent, would not benefit from a course of psychotherapy, that many courts prefer to follow the opinion of a prison doctor on this point. The prison doctor has probably a wider acquaintance with psychiatrists' failures in the field of delinquency than have many psychiatrists.

Yet the fact remains that until prison doctors have some group of letters after their name, they will continue to be vulnerable. I do, however, maintain that the D.P.M. is quite irrelevant to their needs and special work; nor for that matter is there at present any form of special qualification which is appropriate.

Perhaps this is a matter to which the new Institute of Criminology at Cambridge could profitably turn its attention.

ANOTHER PRISON M.O.

MENTAL HEALTH BILL

SIR,—It might interest some of your readers to know that in at least one large mental hospital in the North of England the administration has been handed over to the secretary, and the medical superintendent functions as a consultant psychiatrist with his own medical firm—as do the other consultants.

I understand this arrangement was made, with the particular board's consent, as an experiment for a trial period, and is succeeding so far.

Taunton. MARTIN F. BETHELL.

DEATH FROM TONSILLECTOMY

SIR,—Dr. M. E. N. Smith's article of March 28 is so unusual that one must conclude that you, Sir, intended to stimulate controversy. It amounts to 4 deaths collected for the avowed purpose of condemning the only common factor—placing a patient on a waiting-list for tonsillectomy. The article gives no material on which anyone can estimate the risk of tonsillectomy in given circumstances.

I have dug out of a drawer an article I wrote in 1935 but did not offer for publication. It seems relevant to Dr. Smith's paper and I summarise it here.

In 1934 in the casualty department at the Children's Hospital, Birmingham, nearly 3000 children were operated on by the casualty staff for removal of tonsils and adenoids. All had the quick or guillotine operation under short general anæsthesia (discontinuous or "one-shot" type), as opposed to the long method of deliberate dissection under continuous anæsthesia.

All the children were between the ages of $2^1/_2$ and 12 years and were operated on in batches of from 6 to 13 a day. They were recommended for operation from various sources, including the ear, nose, and throat department, medical and surgical outpatients, and sundry external clinics, so only a few were seen by the operator before the day of operation. The indications for operation, though not always noted, ranged from mechanical obstruction, rheumatism, and sore throats to colds and vague general ill health.

The operations were all part of the routine work of a large casualty department, the same equipment and personnel serving. There was no whole-time theatre staff. The operator was usually myself or a junior resident under supervision. The anæsthetists were mostly recently qualified residents. Ethyl chloride on an open mask was the rule and no atropine was given. After removal of the tonsils and adenoids, the throat was briefly swabbed with either flavine 1/1000 or with 2% 'Dettol'. The routine was to discharge the children next morning.

Complications in 2920 cases were as follows:

Reactionary hæmorrhage	135	(serious 58)
Secondary hæmorrhage	14	
Bronchitis	7	
Lung abscess	1	
Septic throat	3	
Rectal hæmorrhage	1	

This does not include those who may have been taken elsewhere for treatment of complications.

There were no anæsthetic deaths, no deaths from hæmorrhage, and no deaths at any time after the operation known to me. In fact, no anæsthetic death in outpatient tonsillectomy has occurred in this hospital during the past twelve years in 35,000 cases.

Reactionary hæmorrhage was the most distressing complication. Fortunately most cases required merely the removal of a clot from the tonsil bed or no local treatment. Of the 58 severe cases 50 were successfully treated by a post-nasal gauze plug. The remaining 8 cases were re-anæsthetised and either the bleeding points ligatured or the faucial pillars sutured over a swab. No child required blood or intravenous saline. Rectal saline was given in several cases.

Secondary hæmorrhage was never serious or accompanied by gross sepsis.

The 7 children who developed bronchitis within twenty-four hours were considered fit enough to go home forty-eight hours after operation. 1 child was subsequently readmitted with a lung abscess, which resolved satisfactorily.

Mental trauma cannot be assessed properly, for the children were not uniformly reviewed after operation, returning to their respective clinics for examination, but I am convinced that many children's nerves were seriously disturbed by the operation, as shown by histories of screaming fits and anorexia and a great dislike of the hospital.

The tonsil beds were all inspected before discharge and tonsillectomy was found to be complete in over 95%. Less than a dozen children needed reoperation for residual tonsillar poles.

If such a series could be reported without mortality twenty-five years ago in the rather crude conditions of outpatient practice, with large lists, ethyl-chloride anæsthesia given by house-surgeons, guillotine technique, and short stay (twenty-four hours) in hospital, then the risks of operation should be less in present conditions.

Dr. Smith should certainly identify the field from which the deaths were culled, or his conclusions are valueless.

Edgbaston, Birmingham. FAUSET WELSH.

PSYCHOSOMATIC DISORDERS IN CHILDHOOD

SIR,—The paper by Dr. Apley in your issue of March 28 is so pertinent and timely that I am constrained to ask if you cannot find more contributions in similar vein.

Mechanics have their place in medicine, it is true; but a humanistic approach, such as Dr. Apley demonstrates, is so refreshing and so rare that one cannot but regret the degree of attention currently given to the more mechanical aspects of our art and science.

Dr. Apley is to be congratulated on his liberal outlook and the facility and clarity of his presentation. The points which he has raised have struck responsive chords in at least one Western Canadian general practitioner.

North Vancouver, British Columbia. KENNETH M. LEIGHTON.

INFECTION OF PETS

SIR,—May I venture to correct a point in your annotation of April 18? The regulations (S.I.1959/20) to which you refer, "which compel those who sell meat unfit for human consumption as food for pets to cook it and stain it with an indelible dye", were revoked (S.I. 1959/473) just before they were due to come into operation on April 1.

Though it is pretty clear the regulations will be reintroduced later in revised form, we have no assurance that they will be a strengthened version. Indeed, we expect them to be less effective than those now revoked promised to be; and that causes public-health workers considerable concern—not only for the pets!

Health Department, Exeter. E. D. IRVINE Medical Officer of Health.

*** We are grateful to Dr. Irvine for this correction, and we hope that effective regulations will in fact be introduced soon.—ED. L.

Parliament

QUESTION TIME

Anti-poliomyelitis Vaccine

Dr. EDITH SUMMERSKILL asked the Minister of Health what was the reason for the recent maldistribution of poliomyelitis vaccine.—Mr. DEREK WALKER-SMITH replied: Vaccine is allocated on the basis of monthly requisitions from local health authorities, whose estimated needs for the month were delivered by April 4. A very welcome though belated rise occurred shortly after that date in the response from young people, of whom only 1 in 12 had registered for vaccination by the end of February. As, however, it came very suddenly and was unexpectedly steep, a considerable number of local health authorities had to ask urgently for additional supplies of vaccine. These requests have all been met, a million extra doses having been distributed. Further large supplies will be issued to meet the needs of May, including a million doses of imported Salk and the vaccine available from British producers.

Mr. W. R. WILLIAMS: Is it not a reflection on the administration that so soon after a powerful appeal to young people to come forward immediately to be vaccinated against polio, the supply of the vaccine completely broke down all over the country?—Mr. WALKER-SMITH: There was no question of any wholesale breakdown in the country. What happened was that some local health authorities, instead of requiring a preliminary registration, vaccinated on demand at open clinics, first of all in order to encourage young people to come forward and then in order to cope with those large numbers. In doing it on that basis, there were necessarily occasional local difficulties of supply.

Dr. SUMMERSKILL: Is the Minister aware that last week Middlesex County Council told the doctors of Middlesex that promises made to it of supplies of poliomyelitis vaccine had not been fulfilled, that no further vaccine would be available until May, that the only way in which the authority could meet its present commitments was to refuse to give any third injection and that those people who were applying now could be given only one injection?—Mr. WALKER-SMITH: Only one injection is ever given to start with. Then four or five weeks elapse before the second injection is given. I have already said that more vaccine is already going out this month. Dr. SUMMERSKILL: Does the Minister realise that these children were deprived of their third injection which would have given them full protection this summer? The instructions were that the children who were ready for their third injection, which would give them full protection, were not to be given it but that that injection was to be given to new cases.—Mr. WALKER-SMITH: It is within the discretion of each local authority how it arranges its programme. It is obvious that if we get a sudden concentration of demand from young adults it is more difficult to give the third injections to the children at the same time. If there had been a higher registration earlier it would have been easier for local health authorities and general practitioners to carry out the vaccination programme.

Deaths from Tonsillectomy

Mr. JOHN CRONIN asked the Minister of Health how many operations to remove either tonsils or adenoids, or both, were performed in 1958; and how many patients died as a result of these operations.—Mr. DEREK WALKER-SMITH replied: The great majority of the 178,000 patients treated in 1958 in hospital beds set aside for the surgical treatment of tonsils and adenoids are likely to have had operative treatment. The number who died is not known, but provisional figures from the General Register Office indicate that during the year mention of a tonsil and adenoid operation was made on 33 death certificates.

Obituary

JOHN HAY

M.D. Vict., M.D. Lpool, F.R.C.P., D.L.

Prof. John Hay, who died at his home in Bowness-on-Windermere on April 23 at the age of 85, held the chair of medicine in the University of Liverpool from 1924 to 1934, but he had been an influential figure in the medical life of Liverpool almost from the opening of the century.

Burrell & Hardman

As the years went by he occupied every medical position of distinction in Liverpool. But notable as the many academic distinctions were that came to him during his long life, his greatest achievement was the friendly warmth and youthful sincerity of his personality.

His parents were Lowland Scots, Nonconformists and ardent temperance workers—two loyalties that their son maintained all his life. John, the eldest son, was born at Birkenhead, where his father was an architect of considerable distinction. It may seem strange that someone who was so essentially a countryman at heart should have been born in Birkenhead; but in those days it was possible to walk down to the river through green meadows, which now are covered by endless warehouses and traversed by the dock road. Before the turn of the century the family moved to Heswall, at that time a delightful village.

From the Liverpool Institute Hay went to study medicine at the University College of Liverpool, as it then was; and he took the Conjoint diploma in 1895. His early training included the Holt fellowship in physiology, which brought with it early and lasting friendship with Sir Charles Sherrington; a demonstratorship in anatomy which enabled him to enrich the department with wall pictures, in his own hand, of anatomical dissections; a medical registrarship at the Liverpool Royal Infirmary; and a post as pathologist to the David Lewis Northern Hospital. With this basic training, it is not surprising that he was soon appointed as assistant physician to the Stanley Hospital, and the Hospital for Consumption and Diseases of the Chest. He was the first to introduce artificial pneumothorax to Liverpool. On his appointment as assistant physician to the Liverpool Royal Infirmary in 1907, in conformity with the rules, he had regretfully to give up all other appointments. The change, however, enabled him to take a more sustained and concentrated interest in diseases of the heart, and this interest was further enhanced by six months' study at Freiburg.

About this time Hay became a disciple of James Mackenzie, and many were the tales he told his friends years later of those exciting Sunday visits to Burnley. He was openly and unashamedly a hero-worshipper, and he recognised Mackenzie with gratitude as one of his heroes who had significantly influenced the most important stage in his professional life. There is reason to believe that the exchange of ideas was by no means in one direction, from master to pupil, and it is certain that John Hay had much to contribute to the ideas that were fermenting in Mackenzie's mind. The early association ripened into a firm friendship between the two men and their families, which lasted until Mackenzie's death in 1925. Hay was keenly interested in the graphic methods of registration of cardiac activity and much of his early work was on this field. He was also interested in the health and welfare of children and took part in a review which revealed in half the poorer children in Liverpool a degree of malnutrition sufficient to interfere with their education. This review was partly responsible for the start of the school health service.

Shortly before the 1914–18 war he started the heart clinic of the Liverpool Royal Infirmary, the first of its kind in the North of England. This experience led to his appointment soon afterwards as a specialist in cardiac disorders to the First Western General Hospital, and he held the rank of lieutenant-colonel in the R.A.M.C. In 1917 he was appointed full physician to the Royal Infirmary. The war and its aftermath brought many cardiac problems—medical and sociological—and their study and elucidation drew together a small group of distinguished men under the leadership of James Mackenzie. These men, with John Hay among them, were the original members of the Cardiac Club, which was formed in 1922.

The club in due course became the most stimulating and far-reaching influence in British cardiology, and in 1937 it was transformed into the British Cardiac Society. Hay was the oldest surviving member of the original group, and he served as chairman of the society in 1928, 1932, and 1948. At the meetings, especially the informal gatherings associated with them, his sense of fun and wealth of reminiscence kept the younger members alert and thirsting for more, while the older members cancelled their good resolutions for an early bed. The society dinners were not complete without a formal speech, or some informal observations and comments, by John Hay; and even more so without some delightful and easily recognisable caricatures from his own hand. The society elected him an honorary member in 1952, a distinction that gave him particular happiness.

John Hay was a general physician of distinction as well as a cardiologist. He was an original member of the Association of Physicians, served as president in 1948, and was elected an honorary member the following year.

He was also elected an honorary fellow of the Royal Society of Medicine. His exceptionally wide range of medical interests made his advice invaluable in many spheres: he was consulting physician to the Ministry of Pensions, regional consultant adviser in medicine, and chief consultant medical officer to the head office of the Royal Insurance Company. He was also a Deputy Lieutenant of the County Palatine of Lancaster.

As professor of medicine and the senior physician of the Liverpool Royal Infirmary Hay exercised his authority with wisdom and foresight in helping to establish the Associated Voluntary Hospital Board, which later became the United Liverpool Hospitals. In the midst of all these activities he was in consulting practice, and was the leading physician of his day in Liverpool and the neighbouring areas.

His published work was mainly on cardiac research and he also delivered many official lectures.

He gave the Bradshaw lecture of the Royal College of Physicians in 1923, the St. Cyres lecture in 1933, and the Strickland Goodall lecture in 1936. His presidential address at the Liverpool Medical Institution in 1928 was on William Harvey—another of his heroes. His main interests were diseases of the myocardium with special reference to cardiac pain, the arrhythmias, and the treatment of cardiac failure.

Apart from his research he was a constant inspiration and stimulus to other workers in his department. His retirement from the chair in 1934, and his appointment as emeritus professor of medicine, did not lessen his lively interest in the affairs of the infirmary and the university.

E. W. J., to whom we are indebted for this memoir, adds the following personal tribute:

"Many would say that his main distinction was his success as a clinical teacher in the wards and outpatient clinics. He was well grounded in the fundamentals by his comprehensive early training; during those days he carried out personally many postmortem examinations with the direct purpose of correlating the physical signs observed during life with the final pathological findings. It was an invaluable experience for his junior associates to watch him taking a history, and to observe his success in making a friend of a shy or awkward patient. He would ferret out the physical signs with zest and inspire us all with his enthusiasm. To the discussion that followed he brought a keen, analytical, and well-stored mind backed by a wealth of clinical experience, and in conclusion he would recount one of his many humorous and apposite stories designed to imprint the whole case on the memory. As a physician he was remarkably kind and thoughtful, and he would often visit the wards alone to try and unravel a case of unusual complexity, or to help a patient under the stress of emotional or domestic difficulty.

"Extensive as they undoubtedly were, his professional activities were only part of his life, though we often wondered how he found time for anything else. He was deeply imbued with the Celtic love of music and the visual arts. He was a capable musician, and at 75 had to postpone meeting me in consultation over a difficult case, because the time chosen coincided with his music lesson—he was still playing the violin and the viola at that age, and as leader of the family instrumental quartet he had to set them a good example. He was a member of the Liverpool Philharmonic Society, and, until the last few years, never missed their concerts. His sensitive artistic nature also found an outlet in painting, and his delicate water-colours were exceptionally pleasing. The subjects were usually country scenes in his beloved Lake District, or some notable piece of Georgian architecture among the older houses in Liverpool. Many of us will cherish his distinctive Christmas cards drawn by hand. After retiring he took up oil painting with equal success, but his real affection was for water-colours, and he was a president of the Liver Sketching Club. As an enthusiastic photographer he kept a comprehensive record of all his 'firms'. Clinical clerks, sisters, housemen, and registrars signed the famous 'book', the group was photographed, and their later careers were carefully entered. No wonder they all loved him, and his last ward round was the occasion of a demonstration of spontaneous affection and enthusiasm that must have been unique in the long history of the Royal Infirmary.

"His love of the countryside was another real and abiding interest, dating back to early walking tours in Ireland (literally travels with a donkey) and Scotland. Later he developed a deep attachment to the English Lake District that remained to the end of his days, and fell-walking was undertaken with the same enthusiasm as all his other activities. Camping and caravanning were naturally associated with his happy participation in open-air life. In later years he became an expert bee-keeper, and was able to devote time to aid Friends of the Lake District. He had always loved his garden, even in the Liverpool days, but his retirement to the Lake District gave him the time and opportunity that he had long desired for gardening on a more ambitious scale. This ambition was fully gratified, at the cost of hard physical effort, at Knott End and again at Underfell.

"Those of us who visited him at his home in Bowness knew that his supremely active mind had also achieved serenity. The time came when the colours he had loved and captured in his paintings were no longer visible; and the step that had retained its boyish spring for over 80 years, at last, began to falter; his interest in the garden passed imperceptibly from brisk activity to tranquil enjoyment. He faced the increasing limitations and vicissitudes of the last few years with fortitude and equanimity. But in spirit and conversation he remained youthful to the end."

S. A., another of his students, now writes from a Scottish chair.

"No-one ever doubted the wisdom of John Hay's choice of a career. Throughout his long life he combined exceptional ability with an intense interest in the practice of medicine. But there was much more to it than that. He was endowed with those qualities which make a man a leader whether he likes the role or not. He was the empirical physician rather than the clinical scientist, but he preserved a critical and challenging outlook. I once heard a colleague say that G.P.s called in John Hay to tell them what to do when there was nothing more to be done. The comment had a deep significance: John Hay was a man with great reserves. He was largely unaware of the extent of his power because so much of it sprang from the extraordinary radiance of his personality. He didn't need to try to help the patient: it just happened.

"He dressed well. He often wore silver-grey morning dress and a flower in his buttonhole. Nobody thought of this as affectation: this was John and we loved him for it. And anyway he was living in the Age of Elegance which impinged even on the art of prescribing. He belonged to the classic type of Good Physician: sensitive to beauty, repelled by the ugly and uncouth, compassionate, keenly observant, and with a strong sense of duty which made him an exacting chief on ward rounds.

"To those who live amid the sombre greys of the industrial North it was his natural buoyancy of thought and action that brought delight. His physique and temperament seemed to have been cast in the same mould: lively, alert, and generous, his very gestures and deportment proclaimed the joy that came to Diomedes in the company of Cressida:

> "Tis he, I ken the manner of his gait:
> He rises on the toe. That spirit of his
> In aspiration lifts him from the earth."

In 1906, Professor Hay married Agnes Margaret Duncan, who died in 1947. Of their four children, the elder son is professor of child health at the University of Liverpool, and the younger is physician to the Royal Lancaster Infirmary. One daughter is a doctor and the other is married to a doctor.

ARTHUR CECIL ALPORT

M.D. Edin.

Dr. Alport, whose death we announced last week, will be remembered for the excellence of his clinical teaching while he held the chair of medicine at Cairo, and respected for the integrity which led him to resign it.

He was born in South Africa and came to this country to study medicine at the University of Edinburgh. After qualifying in 1905 he practised for some years in Johannesburg. During the 1914–18 war he served in South Africa and later in Macedonia and Salonika, where he treated cerebral malaria by the intravenous and intramuscular injection of quinine. In his book, *Malaria and its Treatment*, which was published in 1919, he described his methods in detail. His war-time work had given him useful practical experience of tropical diseases, and after he was demobilised he became a tropical specialist to the Ministry of Pensions and to the Royal Herbert Hospital at Woolwich.

In 1912 he became assistant director of the medical unit which had just been set up at St. Mary's Hospital. Of his work there W. D. N. writes:

"During the fourteen years that Alport worked on the medical unit there was no introductory course and he gave the junior clerks their first training in clinical methods. He had unlimited patience and willingly gave individual teaching to anyone who found difficulty in hearing and feeling physical signs. Sometimes we told him he was wasting his time casting pearls before swine. He would reply 'even if they are swine now, they will make good doctors by the time I have finished with them' and most of them did. One of his recreations was playing golf, not very well but with great enthusiasm. During

his time at Salonika he had laid out a golf course while draining the mosquito-infested marshes. He was always evolving a new theory about stance or grip and would try it out in the laboratory with a retort stand, sometimes with disastrous results to flasks and beakers."

In 1937 he was appointed professor of clinical medicine in the University of Egypt. His tenure of his chair ended unhappily, for he resigned as a protest against the irregularities which he alleged were then rife in Egyptian hospitals. He also resigned the F.R.C.P., to which he had been elected in 1937. Of this episode a colleague writes:

"Alport's character was downright and honest to a degree which admitted no subtlety or manœuvre. His sympathy for the fellaheen in Cairo led him to attack with his customary directness the bribery which he found existed there; and the obstruction with which his efforts of reform were countered caused him to resign voluntarily from the chair of medicine there, despite an offer of higher pay, and also to take the unusual step of resigning his F.R.C.P., because he failed to obtain the support which he, perhaps irrationally, thought should have been forthcoming from the college."

Alport's resignation, however, successfully won public attention, and in 1944 a Bill for the reform of the medical faculty was brought before the Egyptian legislature.

C. A. P., who during evening hours on the golf course often used to hear his views on life, sums up his personality in these words:

"He was an excellent clinical teacher but no pedestrian crammer, for he had imagination himself and took interest in those he taught. He had many endearing idiosyncrasies, and was quick to recognise and admire honesty and integrity in a man and also to perceive less desirable qualities. Once having made up his mind he had an inflexibility of purpose. He added to medical knowledge, but his real contribution to life was the wise, steadying influence he exerted on men with whom he came in contact. Many are those who remember him with affection."

He died in London on April 17, at the age of 79.

PERCIVAL ELLISON BARBER

Ch.M. Sheff., M.R.C.S.

Dr. Percival Ellison Barber, who died on April 24 at the age of 95, was associated for many years with the Sheffield medical school as lecturer and later as professor of midwifery.

He was a member of a Sheffield family that has had several generations of medical members, and his father was surgeon to the Royal Infirmary. He was educated at Caius College, Cambridge, and St. Bartholomew's Hospital. In 1886 he became an assistant house-surgeon at the Royal Hospital, Sheffield, and house-surgeon in 1889. A visiting dispensary was then run by the hospital and each house-surgeon had to visit patients each day at their own home. Early in his career Barber decided to specialise in obstetrics and gynæcology, so he became a house-surgeon at the Jessop Hospital for Women in Sheffield. Afterwards he entered general practice in Sheffield, and from 1908 to 1921 he was a surgeon on the staff of the Jessop Hospital. He took an important part in the formation and development of the medical faculty in the University of Sheffield, and he was awarded the honorary degree of CH.M. when it was established in 1905. He was appointed professor of midwifery in 1911 and retired from practice in 1921.

Professor Barber leaves a widow, a son, and a daughter.

Births, Marriages, and Deaths

KENYON.—On April 4, at Queen Charlotte's Hospital, London, to Nuala and Islay Kenyon, a daughter—Nuala Rose Catriona.

Diary of the Week

MAY 3 TO 9

Monday, 4th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
8.15 P.M. *Epidemiology & Preventive Medicine.* Prof. J. E. Salk (Pittsburgh): Vaccination Against Poliomyelitis—How Much is Enough?

POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W.12
4 P.M. Mr. Geoffrey Knight: Surgical Treatment of Mental Illness.

WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospital Medical School, W.2
5 P.M. Prof. P. B. Beeson (Yale): Studies on Bacterial Infections of the Kidney. (Almroth Wright lecture.)

Tuesday, 5th

UNIVERSITY OF LONDON
5.30 P.M. (University College, Gower Street, W.C.1.) Prof. V. B. Mountcastle (Baltimore): The Central Nervous Mechanisms in Somatic Sensation. (First of two lectures.)

ST. MARY'S HOSPITAL MEDICAL SCHOOL
5 P.M. Dr. Desmond O'Neill: Tension Pain in Gynæcological Practice.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY, 91, Dean Street, W.1
5.30 P.M. Mr. Joseph Minton: Ocular Manifestations in Clinical Neurology. (Second of two lectures.)

WEST OF ENGLAND CHILD HEALTH GROUP
5.30 P.M. (Children's Hospital, Bristol.) Dr. Cecile Hopkins: Problem Families.

UNIVERSITY OF LIVERPOOL
5.15 P.M. (Liverpool Medical Institution, 114, Mount Pleasant, Liverpool, 3.) Dr. Robert Coope: Medicine in the Early Nineteenth Century.

Wednesday, 6th

UNIVERSITY OF LONDON
5.30 P.M. (London School of Hygiene and Tropical Medicine, Gower Street, W.C.1.) Professor Salk: Waxing and Waning of Epidemics in Our Time.
6 P.M. (Bedford College, Regent's Park, N.W.1.) Dr. D. J. van Lennep (Utrecht): Recent Studies on the Personality of the Proficient Research-worker. (First of two lectures.)

ROYAL SOCIETY OF MEDICINE
5.15 P.M. *History of Medicine.* Dr. W. H. McMenemey: John Conolly (1794–1866), the Reformer.

POSTGRADUATE MEDICAL SCHOOL
2 P.M. Dr. E. J. L. Lowbury: Infection of Burns.

INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Sir Russell Brock: The Present Position of the Surgery of Pulmonary Stenosis With Normal Aortic Root.

INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. Henry Haber: Lymphocytic Infiltration of the Skin.

ASSURANCE MEDICAL SOCIETY
5 P.M. (11, Chandos Street, W.1.) Dr. Francis Bach: Rheumatic Diseases and Their Relation to Life Insurance.

MANCHESTER MEDICAL SOCIETY
5 P.M. (Medical School, University of Manchester.) Prof. M. L. Rosenheim: A Medical Visit to the Antipodes.

Thursday, 7th

UNIVERSITY OF LONDON
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. François Jacob (Paris): Viruses in Relationships With Some Genetic Elements of the Cell.
5.30 P.M. (University College.) Professor Mountcastle: Central Nervous Mechanisms in Somatic Sensation. (Second of two lectures.)
6 P.M. (Bedford College.) Dr. van Lennep: Recent Studies on the Personality of the Proficient Research-worker. (Second of two lectures.)

ROYAL SOCIETY OF MEDICINE
8 P.M. *Neurology.* Dr. W. Ritchie Russell, Prof. Norman Dott, Dr. P. W. Nathan: Treatment of Intractable Pain.

POSTGRADUATE MEDICAL SCHOOL
4 P.M. Dr. Raymond Daley: Mechanism and Treatment of Cor Pulmonale.

INSTITUTE OF NEUROLOGY, The National Hospital, Queen Square, W.C.1
5 P.M. Professor Dott: Syndromes of Cerebral Displacement.

BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, W.1
8 P.M. Dr. J. Blair Hartley: Blind Spots—First Rib Stresses—and the B.I.R. (Presidential address.)

NUFFIELD ORTHOPÆDIC CENTRE, Wingfield-Morris Orthopædic Hospital, Oxford
8.30 P.M. Dr. J. Judet: Treatment of Talipes Equino-varus in Children Beyond the Age of Two Years.

HONYMAN GILLESPIE LECTURE
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Prof. H. N. Robson: Aspects of Leukæmia.

UNIVERSITY OF ST. ANDREWS
5 P.M. (Queen's College, Small's Wynd, Dundee.) Dr. F. H. Kemp: Radiographic Studies of the Pharynx and Larynx.

Friday, 8th

POSTGRADUATE MEDICAL SCHOOL
10 A.M. Mr. W. T. Irvine: Clinical and Experimental Problems of Ureteral Transplantation.

FACULTY OF RADIOLOGISTS
4.30 P.M. (Royal College of Surgeons of England, Lincoln's Inn Fields, W.C.2.) Dr. S. Cochrane Shanks: Medicine, Radiology, and The Law. (Knox lecture.)

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
3.30 P.M. Dr. D. A. Osborn: Blood Disease in Ear, Nose, and Throat Conditions.
5.30 P.M. Mr. Norman Asherson: Cysts of the Larynx and Pharynx.

BRITISH SOCIETY FOR IMMUNOLOGY
11 A.M. (London School of Hygiene and Tropical Medicine.) Symposium on Delayed Hypersensitivity. Opening of two-day meeting.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH, Edinburgh, 8
3.30 P.M. Prof. J. B. Kinmonth: Aspects of Cardiovascular Surgery.

Notes and News

AGAINST RHEUMATISM

Two years ago the *Empire Rheumatism Council* made a national appeal to raise a £250,000 research fund. So far £135,500 has been collected, and with this encouraging support the Council in 1958 spent £25,000 on medical projects, and plan to raise their expenditure to £37,000 in 1959. In the report [1] for 1958 Dr. Oswald Savage, the hon. medical secretary, surveys the help which the Council has given to research.

The population studies in Lancashire have been extended with the help of the Wellcome Foundation's mobile X-ray department and laboratory. Further field surveys are also being made in the Rhondda Valley in Wales and in Wensleydale in Yorkshire.

Investigations into the structure of the connective tissues include Dr. Paul Fourman's investigation at Cardiff into the effect of injecting substances such as chondroitin sulphate and hormones of the parathyroid glands on organs such as the kidney and blood-vessels. In Birmingham Prof. J. R. Squire has begun to study blood-proteins with the ultracentrifuge and by immunochemical methods. Work on osteoarthritis includes Dr. M. Wilkinson's study of changes in the cervical vertebræ and Prof. D. H. Collins' on the metabolic activity of hyaline cartilage. Among the studies of new drugs are Dr. D. Abelson and Dr. I. C. Gilliland's investigations into the rate of disappearance of hydrocortisone from the blood and Dr. V. Moses' of the effect of salicylates on the chemical changes in tissue.

The chief aim of the *British Rheumatic Association*, which was founded ten years ago, is to help rheumatic patients "to overcome their disabilities and to remain active and useful members of the community", and in its eleventh report [2] it is able to record further useful work.

The future of the Royal National Hospital for Rheumatic Diseases at Bath, thanks in part at any rate to the efforts of the Association, seems now to be assured and it is hoped that in the coming year the bombed wing will be rebuilt. The treatments centre, which the Corporation of Bath runs as the agent of the hospital and of the National Health Service, is on the ground floor of the former Grand Pump Room Hotel, and the Association is considering leasing the two upper floors and converting them into a hostel for people who come from other parts of the country to attend the hospital as outpatients. The Association is already gathering funds for this purpose and, though the welfare department has this year again allocated over £1000 in grants, it has added some £2000 to its reserves.

MENTAL HEALTH OF THE FAMILY

CONSULTANT psychiatrists and senior medical officers in the public-health service from all over the country met recently at a five-day seminar arranged by the mental health group of the Society of Medical Officers of Health at the London School of Hygiene and Tropical Medicine.

The opening address was given by Sir John Charles, chief medical officer of the Ministry of Health, and the theme of the conference "Planning for the Mental Health of the Family" was introduced by Dr. Noel Harris, president of the group. The seminar covered future mental-health planning for individual age-groups and the family as a whole, and considered broad principles of cooperation. The following conclusions were reached:

Public and mental health services must be jointly planned to meet the sociomedical needs of the family from the antenatal period to old age. The training of midwives must include consideration of emotional factors during pregnancy and the puerperium. The good nursery school was regarded as a possible means of helping the emotional and social development of some children, especially if arrangements could be made for the parents to cooperate constructively.

Not all children are ready for full-time education at the age of 5, and greater flexibility in the admission policy to schools may be indicated. Problems of adolescence offer scope for parents as well as guidance through public-health staff, the education services, and the family doctor. Pilot schemes of open-access clinics, similar to those set up in the Boston experiment, might be introduced in some areas.

Dr. J. A. Gillet, medical officer of health for Dagenham, reported on a scheme, supported by the general practitioners in this area, to give old people not only medical supervision and exercises designed for their particular needs, but also to teach them the part they can play in the family and the community.

The most important and immediate problem is the training of public-health staff and family doctors in the field of mental health. This can only be tackled by allocating some of the psychiatrists' time for training the medical, nursing, and social-worker professions, and in this way closer links will be established between mental and other health services. The case-conference method of in-service training advocated by the county council study group [1] was strongly supported. Another step in the right direction was the recent recommendation [2] that, by part-time secondment, the trainee psychiatrist or registrar should become acquainted with the public-health field, and that new entrants to the public-health service should have experience in the three main branches of psychiatry—i.e., child psychiatry, mental illness, and the subnormalities.

1. Obtainable from the Council, Faraday House, 8, Charing Cross Road, London, W.C.2.
2. Obtainable from the Association, 11, Beaumont Street, W.1.

NEW BUILDINGS AT THE CENTRAL MIDDLESEX HOSPITAL

THE National Health Service was never intended to stifle the great tradition of voluntary service in this country's hospitals, said Mr. Maurice Orbach, M.P., chairman Central Middlesex Group Hospital Management Committee, at a ceremony held at the hospital on April 21. Three new buildings were formally opened on this occasion—a shop to serve both staff and patients, a diet-kitchen for the gastroenterological unit, and a central sterilising service.

Lord Cottesloe, chairman of the North West Metropolitan Regional Hospital Board, pointed out that quality in medicine was not necessarily proportional to the appearances of the buildings in which it was practised. Since the National Health Service started, thirteen different schemes had been completed in the hospital, and the £165,000 these had cost was a substantial proportion of the Regional board's total expenditure on building. Moreover, a tender to provide greatly enlarged casualty, outpatient, pathological, and radiological departments for the hospital had recently been authorised. These buildings would cost £167,000 and he hoped that work would begin later this year.

Mr. Leslie Farrer-Brown, director of the Nuffield Foundation, thought that the Central Middlesex Hospital was surely a model for others to copy. He paid tribute to the hard work and many-sided research carried out in the gastroenterological unit under the direction of Dr. Avery Jones.

The new shop is cheerful in appearance and makes good use of modern materials. King Edward's Hospital Fund for London contributed £2500 towards the cost of this, and the remainder was found by the League of Friends of the Hospital. All profits from the shop are to go towards building a large general lounge for the patients and their visitors.

The new diet-kitchen, planned after suggestions from all who work there, is spacious and airy, and is decorated in pale blue and primrose. At present it is preparing between eighty and a hundred diets daily, but eventually, when the new general kitchens have been built, its work is to be confined to the more specialised diets required by the gastroenterological unit. The Nuffield Foundation contributed £2060 and the regional hospital board £2500 towards the cost of the kitchen.

The sterile-service department—which is for the whole hospital group and not the Central Middlesex Hospital alone—has not yet been completed, and a fresh appraisal of sterilisation techniques is to be undertaken. Above this department, however, new suites for consultants have been provided, and these rooms, with their fitted carpets and walls painted in contrasted colours, should do much to house the physicians and surgeons better.

APPARATUS FOR THE DISABLED

THE National Fund for Poliomyelitis Research has set up a committee for research on apparatus for the disabled, under the chairmanship of Sir Harry Platt. The other medical members are Dr. D. A. Brewerton, Mr. Norman Capener, Dr. W. F. Floyd, Dr. A. B. Kinnier Wilson, Dr. D. S. McKenzie, Dr. J. F. Scales, and Dr. H. Beric Wright. The

1. *Medical Officer*, 1954, **92**, 303.
2. *Lancet*, April 4, 1959, p. 728.

committee will consider how apparatus can be developed by doctors and engineers working in partnership, and how the physical capabilities of the patient and nursing aids can be improved by using modern engineering methods and the resources of industry. At the Institute of Orthopædics' poliomyelitis centre a team of Medical Research Council workers are already studying problems of handling the severe cripple, and the fund has made a grant of £19,000 for an initial three-year period towards this project.

CIVIL SERVICE SALARIES

THE increases in the pay of the higher Civil Servants which were recommended by the Coleraine Committee earlier this year have been approved by the Government. They will take effect from Feb. 1, and they will affect the following medical appointments:

—	Current (London) rates	New rates
	£	£
Chief medical officer (Ministry of Health) ..	5000	5800
Above principal medical officer (broadbanded)	3400–3750	3800–4400
Principal medical officer	3000	3300
Senior medical officer	2700 (flat rate)	3000

University of London

Dr. Charles Wilcocks, director of the Bureau of Hygiene and Tropical Medicine, has been appointed Heath Clark lecturer for 1960.

At a meeting of convocation to be held at 6 P.M. on Tuesday, May 12, at the Senate House, Malet Street, W.C.1, the guest speaker will be Dr. C. F. Harris, the vice-chancellor. His subject will be problems of medical education.

The following degrees have been conferred:

M.D.—William Brumfitt, John Pryse-Davies, H. C. Smellie, N. A. F. Young.

M.S.—Irene M. S. Cade, D. B. Griffiths.

Ph.D. (in the faculty of medicine)—Satish Chandra Agarwal, Ranjit Sen.

University of Leeds

On Wednesday, May 20, at 5.15 P.M., at the General Infirmary, Leeds, Dr. Peter Miescher, of the University of Basle, will give a lecture on the pathogenesis of lupus erythematosus.

University of Edinburgh

Prof. E. C. Mekie has been appointed director of studies to the Edinburgh Post-Graduate Board for Medicine in succession to Sir Alexander Biggam.

Professor Mekie, who is 57, was educated at George Watson's College and the University of Edinburgh, where he graduated M.B. in 1925. In 1928 he was appointed assistant in the department of clinical surgery under Professor (later Sir John) Fraser. From 1933 to 1935, with an Ernest Hart scholarship, he carried out research in the Wilkie laboratory, and acted as surgical specialist to Scottish Command. The next twenty years he spent in the Far East where he held successively the chairs of clinical surgery and surgery in the University of Malaya. He was consulting surgeon at the Civil General Hospital, Singapore, and also surgical consultant, Far East Command, R.A.M.C. and R.A.F. Since his return to Britain in 1955, Professor Mekie has been conservator of the museum at the Royal College of Surgeons of Edinburgh.

Dr. P. G. Fawcett and Dr. Ian Oswald have been appointed lecturers in psychological medicine.

University of Glasgow

The degree of M.D. has been conferred on the following:

James Crooks (with honours), S. P. Smith (with commendation), H. R. F. Macdonald, W. G. Manderson, A. J. S. McFadzean (in absentia).

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting of the faculty on April 6, with Mr. Arthur Jacobs, the president, in the chair, the following were admitted to the fellowship:

William Chan, J. S. Eapen, William Hamilton, J. D. Kinloch, J. K. G. Macarthur, P. D. Moylan, Narendra Kumar Sinha (qua physician), Shedden Alexander, J. P. Galloway, Sankara Gopala-Pillai, S. Srinivasa Rao, Calapatti Ramaswami Subramaniam, J. R. Thomson (qua surgeon).

University of Dublin

Prof. R. J. V. Pulvertaft has been appointed John Mallet Purser lecturer for 1959.

Royal Society

The four foreign members of this society elected on April 23 included Prof. Gerard Domagk, of the University of Münster, and Prof. A. H. T. Theorell, of the Nobel Medical Institute, Stockholm.

British Congress of Obstetrics and Gynæcology

Applications for membership of this congress, which is being held in Cardiff from July 14 to 16, should be sent without delay to the hon. secretaries of the congress, The Maternity Hospital, Glossop Terrace, Cardiff.

Association of Occupational Therapists

This Association will hold a congress from May 7 to 9 at Church House, Westminster. Further particulars may be had from the organising secretary of the Association, 251, Brompton Road, London, S.W.3.

First International Congress on Irradiation of Endocrine Organs

This congress will be held from May 30 to June 2 in Amsterdam. Further particulars may be had from Dr. Johanna M. van Went, Banstraat 30, Amsterdam Z 1, Holland.

District Nurse Training Today and Tomorrow

The Queen's Institute of District Nursing will hold a conference and exhibition on this subject on Thursday, May 21, at the Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2. The speakers will include Dr. R. W. Elliott, who will speak on what the community expects of the district nurse. Further particulars may be had from the general secretary of the institute, 57, Lower Belgrave Street, S.W.1.

Dr. D. A. Long has been appointed chief medical adviser and head of the medical research department of the Wellcome Foundation Limited. He has been a member of the staff of the Medical Research Council at the National Institute for Medical Research since 1948.

Mr. J. P. Monkhouse has been appointed honorary consultant in otology to the Royal Air Force.

Prof. W. C. W. Nixon has been appointed World Health Organisation consultant in obstetrics and gynæcology to the University of Ceylon for the months of June to August.

A meeting for general practitioners will be held on Sunday, May 3, at 10.15 A.M., at University College Hospital, Gower Street, London, W.C.1, when Prof. M. L. Rosenheim will give a clinical demonstration on nephritis.

CORRIGENDUM: *Council Election of Royal College of Surgeons of England.*—In our issue of April 25 (Advertisers' Announcements, p. 42) the name of Robert Victor Cooke was wrongly given as Herbert Victor Cooke.

Appointments

BAMFORD, C. R. B., M.B. Durh.: school M.O., Northumberland.

CLAYTON, B. E., M.D. Edin.: consultant pathologist-in-charge, department of chemical pathology, The Hospital for Sick Children, Great Ormond Street, London.

FARMER, MADGE, M.B. Lpool: assistant divisional M.O., Lancashire County Council (Lancaster area).

ROLLASON, W. N., M.B. Birm., F.F.A., D.A.: consultant anæsthetist, to take charge of anæsthetic services, North-Eastern Regional Hospital Board, Scotland.

SMITH, R. B., M.B. Edin.: school M.O., Northumberland.

TILL, KENNETH, M.B. Cantab., F.R.C.S.: consultant neurosurgeon, The Hospital for Sick Children, Great Ormond Street, London.

VIGNOLES, J. F. H., M.B. N.U.I.: assistant divisional M.O., Lancashire County Council (Burnley and Nelson area).

Leeds Regional Hospital Board:

GORE, C. P., M.D. Dubl., M.R.C.P.I., D.P.M.: consultant in psychiatry, Scalebor Park Hospital, Burley-in-Wharfedale.

MEIKLE, R. W., M.B. Glasg., M.R.C.P.: consultant in general medicine, Goole, Selby, and Wakefield areas.

SMITH, CHARLES, M.B. Lond., F.R.C.S., D.L.O.: part-time consultant in otolaryngology, York area hospitals.

South-Western Regional Hospital Board:

BRADFIELD, A. M., M.B. N.Z., M.R.C.P., D.P.M.: assistant psychiatrist (S.H.M.O.), Bristol mental hospitals group.

DONLY, L., M.D. Warsaw, D.P.M.: assistant psychiatrist, Bristol mental hospitals group.

HERON, W. C., M.B. Belf., F.F.R., D.M.R.D.: consultant radiologist, Exeter.

JONES, I. S., M.B. Cantab., F.R.C.S.: consultant general surgeon, Plymouth.

WARREN, P. K. G., M.B. Lond., M.R.C.P., D.P.M.: assistant psychiatrist, Bristol mental hospitals group.